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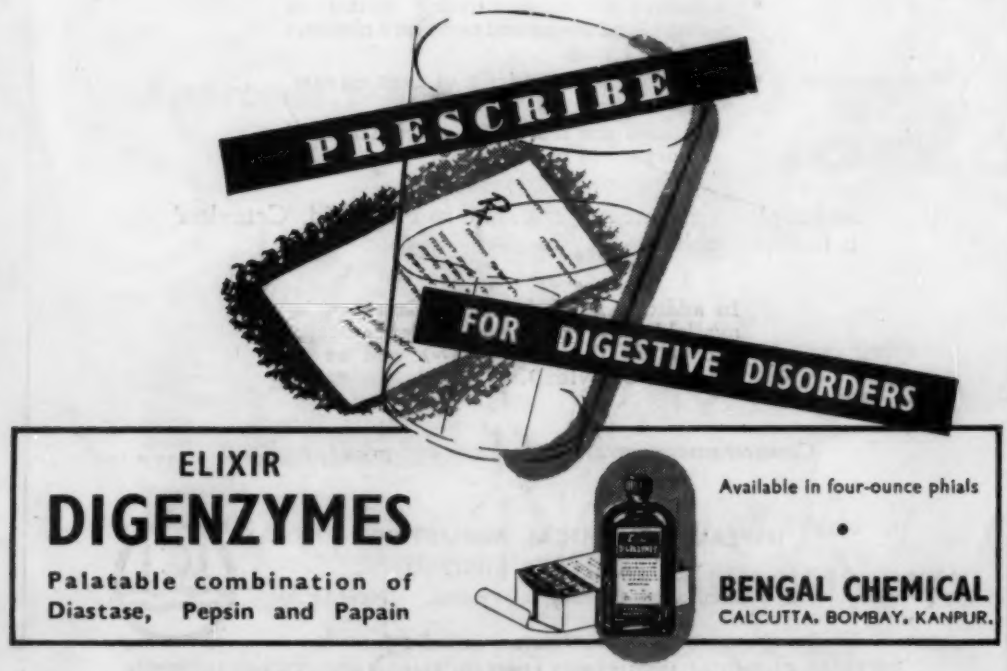

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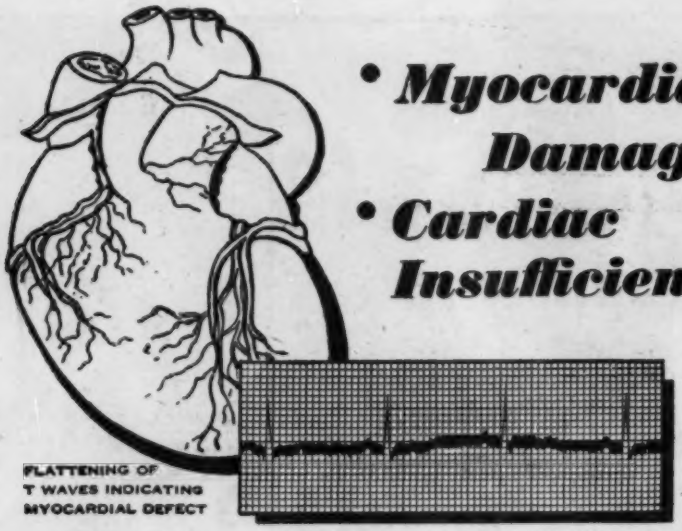

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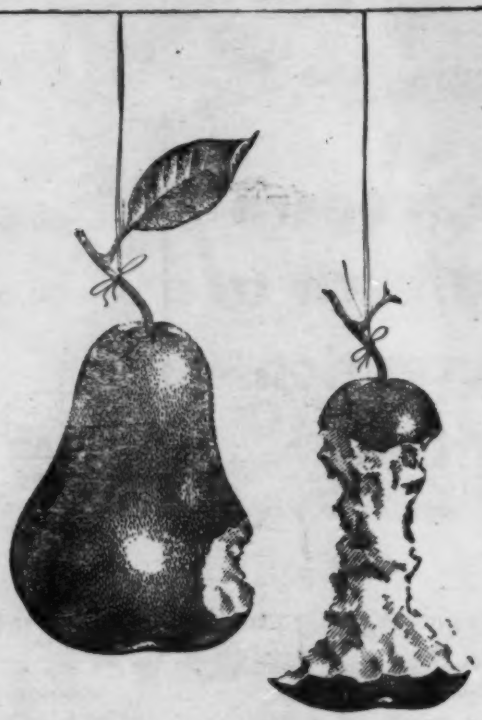

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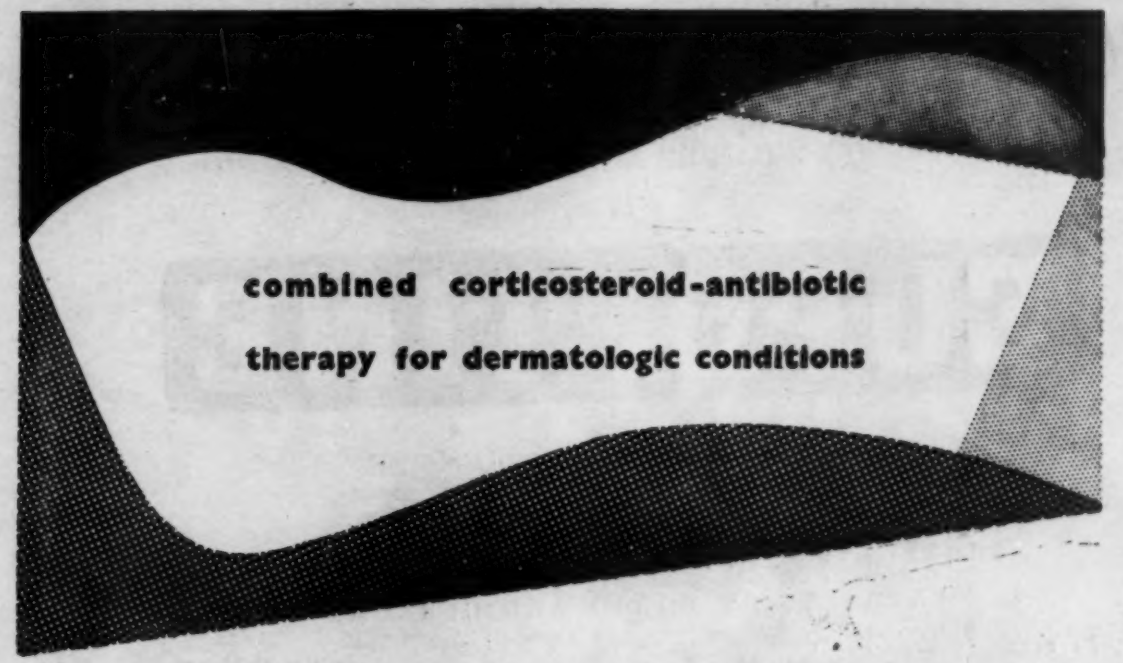

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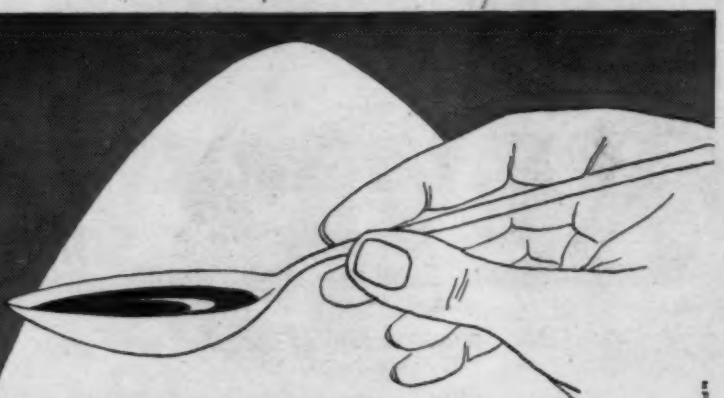

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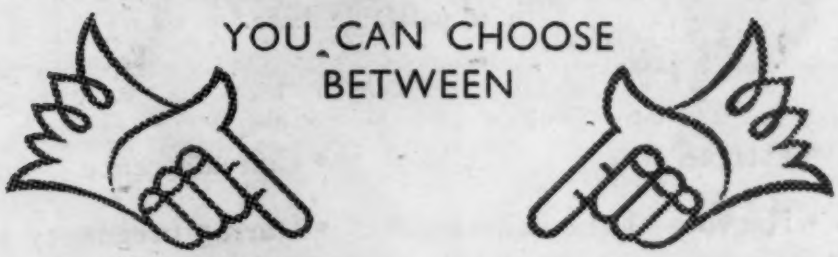

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EDITOR—P. K. GUHA, M.B., M.R.C.S. (ENG.), D.O.M.S. (LOND.)

CALCUTTA
OCTOBER 16, 1957

ORIGINAL ARTICLES

INTRALOBAR BRONCHOPULMONARY SEQUESTRATION

Review of Literature and a Case Report

NEWMAN L. STEPHENS, M.D. (MED.)

Department of Medicine, Clara Swain Hospital
Bareilly

INTRODUCTION

The subject under discussion concerns the heretofore relatively rare pulmonary congenital defect known as intralobar bronchopulmonary sequestration. I have been prompted to report a case and discuss some aspects of its embryology and pathogenesis, least of all because of its rarity, but, preponderatingly because the advent of thoracic surgery in India is bound to reveal more such cases in the future, because failure to recognise the condition leads to ineffective medical treatment (as occurred in the case to be reported) or to disaster at surgery, and because it must be considered in the differential diagnosis of basal cavities.

It is chiefly the impetus provided by thoracic surgery which has been responsible for the emergence of pulmonary sequestration as a clinical entity. This differs radically from what obtains in the case of another allied condition known as extralobar sequestration or inferior accessory lung, which has achieved recognition chiefly as the result of necropsy studies, and which may sometimes resemble intralobar sequestration.

To define it as Bruwer *et al* (1954) have done, in intralobar bronchopulmonary sequestration there is partial or complete developmental separation of a portion of the lung from its contiguity with the bronchial tree. Almost invariably a lower lobe is involved, and the subsegment usually affected is in the posterior basal region. The sequestered area is usually the site of cystic changes and may or may not be infected. The involved segment is supplied by a large artery which arises from the aorta, usually immediately above or below the level of the diaphragm.

The arterial anomaly may be of the following three types:

(1) It may arise from the aorta either above or below the diaphragm as just mentioned.

(2) It may be a branch of an intercostal artery.

(3) It may be a contribution from both the aorta and the intercostal artery. The vessel may be single or it may be represented by a leash of vessels (Boyd, 1953). Its venous drainage is usually into the pulmonary vein.

PATHOLOGY

The gross abnormality is found to fall into one of the three groups of Pryce as quoted by Clagett *et al* (1954):

(1) A large cyst in the sequestered area.

(2) A polycystic mass.

(3) A sequestered mass which contains bronchi that branch parallel to the anomalous artery.

In any of these gross types, the bronchial or alveolar elements may be completely dissociated from the bronchial tree, or there may be a small communication, perhaps as the result of infection,

as postulated by Kergin (1952). Polycystic specimens may thus communicate with adjacent normal bronchi or be totally isolated and filled only with a jelly-like substance, probably inspissated mucus. There is no evidence of alveoli in the tissues surrounding the cysts and no evidence of pigment in the sequestered segment. It seems that the bronchi are dilated into cysts and the alveoli are undeveloped. The tissue between the expanded bronchi is largely fibrotic, with variable numbers of inflammatory cells, depending on the amount of infection which has gained access by contiguity from infected adjacent lung, or by haematogenous spread. The anomalous artery usually enters the lung in the region of the lowermost limit of the pulmonary ligament. Large lymph nodes free of any pigment sometimes occur in the region of this 'accessory hilum'. The anomalous artery has been said to be of the bronchial type. Pryce (1947) has indicated that it has the histology of a true pulmonary artery. Frequently intimal sclerosis is present.

Germane to the discussion and understanding of the pathogenesis of this condition is an exposition of certain points of pulmonary embryology. The embryonic gut is supplied by the rich splanchnic plexus which connects with the dorsal and ventral aorta. The pulmonary bud differentiates in the 4 mm. embryo from the foregut. It retains a blood supply from the splanchnic plexus which constitutes Huntington's so-called 'post-branchial pulmonary plexus'. The developing pulmonary artery which has arisen from the sixth aortic arch joins this plexus. A possibility for the emergence of anomalous arteries from the aorta to the lung exists when branches between the dorsal aorta and the splanchnic and Huntington's plexus persist.

Pryce (1947) who is closely associated with the drawing of attention to, and hypothesising a theory of pathogenesis for, intralobar broncho-pulmonary sequestration indicates that the persistence of the anomalous artery is the cause of the sequestration. According to his theory, the artery during foetal development captures one or more bulbous tips of the embryonic bronchial tree. Traction is then exerted on these sequestered bronchial buds, anchored by the aberrant artery and by the normal lung shifting from its original position in the region of the septum transversum. The extent of the deficiency in the normal lung is uncertain and the absence of such deficiency is in some cases explained by the ability of the normal lung to make good the deficiency as indicated by Flint's work. The lung changes are considered to be the result of continued traction by the aberrant vessel in its embryonic capillary form.

The reverse opinion has also been subscribed to by those like Bolck quoted by Abbey Smith (1956) who feel that the sequestration of the pulmonary tissue developed first and that the tissue then obtained a blood supply from the region in which it lay.

Tosatti and Gravel (1951), Weisel, Docksey and Glicklich (1955), feel that the lesion is really a bronchial cyst and the abnormal artery is a separate additional defect.

Mention must be made of the work of Cole, Alley and Jones (1951) who relate bronchogenic cysts, so-called intralobar sequestration and inferior accessary lungs and diaphragmatic defects as allied conditions and nebulously depute the reason to 'some interference with embryologic development in that area.'

Abbey Smith (*loc. cit.*) has struck out on a different line of reasoning and as the result of minute study of his own clinical material and critical analysis of that of others, postulates that the primary lesion in intralobar sequestration is some failure of the pulmonary artery in foetal life to supply the segment of lung involved. The reasons for this failure are not definable in precise terms. His theory supposes that because of this defect the systematic embryonic supply to the foetal lung persists (i.e. from the postbranchial plexus previously mentioned) and as a result of the systemic pressure and the high oxygen content of this aortic vessel, lung changes arise after birth in the area of the lung to which this supply is distributed.

Abbey Smith (*loc. cit.*) was led to study the problem afresh on the basis of two observations:

(1) The pulmonary artery to the lower lobe on the side of the lesion was at operation found to be greatly reduced in size and the aberrant and the usual pulmonary circulations seemed to be separate.

(2) The lung changes were intimately related to the distribution of the artery.

He puts forward three explanations for the production of lung changes by the artery: (a) because the artery carries oxygenated blood and because of its aortic origin it may cause hypertrophy of the mesenchymal elements of the lung at the expense of the alveolar components. (b) Cudkowicz and Armstrong (1953) found that in cases of pulmonary emphysema associated with occlusion of the pulmonary artery and an aberrant systemic (bronchial) supply to the lung, degeneration of the

lung and fibrosis in the area supplied by that vessel occurred, and this simulates almost exactly what is occurring in cases of intralobar sequestration ; (c) some observers have pointed out that in foetal life some eighteen generations of bronchi are formed and after birth seven more generations of buds develop. It is possible that after birth if a systemic vessel supplies some of the newly developing segments, cystic changes and fibrosis may set up because of this vessel carrying a high oxygen concentration. Before birth this systemic supply would cause no defect.

To date about 100 cases of intralobar bronchopulmonary sequestration have been reported in the foreign literature and to the best of my knowledge no case report has appeared in Indian literature. The purpose of this paper is to document another such case and to formulate another theory of pathogenesis based on a concept of Mayer and Rappaport (1952) with reference to the developmental origin of cystic lung disease, bronchiectasis and emphysema. Knowing that cystic changes, bronchiectasis, fibrosis and emphysema occur early in children suffering from fibrocystic disease of the pancreas, xanthomatosis, tuberous sclerosis of the lungs and pulmonary scleroderma, it can be inferred that the developmental deficiency in all these conditions may be a true hypoplasia, because of inherent weakness, or because of autonomic dysfunction resulting in disturbances of blood supply, and of myoelastic bronchial function. These would produce changes in the lung during early life at a time when new and susceptible bronchial bud generations were still developing. It is likely that what is occurring in a more generalised fashion in the conditions detailed above, may occur in a localised fashion in sequestered lobes of the lung.

It was mentioned in previous paragraphs that extralobar sequestration may sometimes be confused with intralobar sequestration. Table 1 shows the main differences between the two.

Finally it needs to be stated that whilst the sequestered lobe can be infected from adjacent lung with the usual pathogenic bacteria, tuberculosis had not been reported till Boyd (1953) described two cases. Confronted with a basal tuberculous cavity, one should entertain the possibility of the underlying lesion being a sequestration, especially when the usual predisposing factor like diabetes is absent.

As far as the clinical picture is concerned, some cases, albeit a few, are found on routine chest x-ray. The majority of cases occur in children or young adults. In symptomatic cases the history presents symptoms of repeated episodes of infection

TABLE 1—SHOWING THE DIFFERENCES BETWEEN INTRALOBAR AND EXTRALOBAR SEQUESTRATION

Intralobar sequestration	Extralobar sequestration (Accessory lung)
Usually occurs on the left side to the extent of 50 per cent or slightly more.	Almost always on the left side to the extent of 90 per cent or so.
Diagnosis overlooked in some cases; diagnosis is suspected at 6-12 years of age when symptoms set in, and confirmed at surgery.	Patients do not survive the first month and so the diagnosis is made at post-mortem.
Sequestered lobe lies within the substance of the lung.	Sequestered lobe can be seen distinct from the lung.
Artery to the sequestered lobe is large and arises from the aorta either above or below the diaphragm. The return flow is to the pulmonary vein.	Artery to the lobe is small and has an inconstant source. The venous return is to the hemiazygos vein.
No other congenital anomaly co-exists, the lobe has no attachment to the foregut.	Other congenital anomalies are also found and attachment to the foregut occasionally occurs.

and suppuration in a lung cavity, with fever and chills, cough with a moderate amount of sputum, a reduced incidence of foetor, and, small haemoptyses off and on. Usually the cases have been repeatedly treated for lung abscess or bronchiectasis with pneumonitis. Surgical drainages will probably have been attempted. If the cysts have no connection with the rest of the bronchial tree, on the plain skiagram a solid mass is seen at the lung base, however, the lateral view usually presents a 'misty outline' of the lesion. Sometimes the mass seems to point in the direction from which the aberrant artery has arisen, viz., towards the aorta. Fluid levels are seen in those cases where the cysts have a connection with the rest of the bronchial tree. Bronchograms show that the lipiodol has not entered the cystic area. In one of the six cases reported by Boyd, five attempts made at bronchography to visualise the affected cysts were all fruitless.

CASE REPORT

Patient V.B., aged 15 years, a single Hindu male coming from Sitapur was admitted to the Clara Swain Hospital on 18-2-1956 with the complaints of fever and cough with expectoration in recurring bouts since 1948 when he was 8 years of age. The bout in 1948 was con-

trolled with some treatment whose nature is not remembered. Six months later he experienced a similar bout which lasted for two months and was associated with a generalised skin eruption and considerable weight loss.

In 1953 x-ray showed a polycystic posterior basal segment. A radiological diagnosis of bronchiectasis was made. It was also thought to be a case of lung abscess, for which he received penicillin and streptomycin injections and aerosol penicillin with partial relief. Thereafter he maintained indifferent health punctuated by episodes of fever with cough and slight expectoration. Various broad spectrum antibiotics were exhibited from time to time with transient amelioration. The family history was barren of any tuberculous contacts.

On admission he was running a temperature of 99°F. He was in fairly good general health and was not toxic. Physical signs in the chest were not remarkable, a diagnosis of right basal bronchiectasis was arrived at on the basis of fluoroscopic findings and the history.

Laboratory examination—Sputum negative for A.F.B. on 3 separate occasions. Hb. 17·5 g. per cent. R.B.C. 5·2 m./c.mm., W.B.C. 12,600/c.mm., polymorphs 75 per cent, lymphocytes 23 per cent and eosinophils 2 per cent. E.S.R. 1 hour—13 mm. (Wintrobe). Kahn was negative.

X-ray report—"There is very slight blunting of the right costophrenic angle. The bronchovascular markings are specially exaggerated in the mid lung field, off the right hilum. At the right base just above the dome of the diaphragm there is a cystic area about 4 cm. in diameter. No fluid is seen in the cyst (Fig. 1, *vide* Plate). A diagnosis of cystic disease of the right lower lobe was made and a bronchogram advised to rule out additional bronchiectasis not seen in the plain x-ray.

Indirect laryngoscopy—Larynx, epiglottis and cords normal.

Bronchoscopy and *bronchography* reports were as follows—Endoscopic examination 8 x 40 scope passed. Essentially normal tracheobronchial tree.

20 c.c. lipiodol instilled into the right bronchial tree. The p.a. and lateral bronchograms reveal good filling of the main bronchi without any filling defect (right lung). The cystic area noted at the right base does not fill giving the impression of a blocked bronchus. The diagnosis was now of a cyst of the right lower lobe with no evidence of bronchiectasis. A right lower lobectomy was advised.

At this stage the possibility of the lesion being due to sequestration was entertained. The patient went home for a few days and was readmitted on 16-3-1956 for resection. The laboratory reports (18-3-1955) were: Hb. 16·5 g. per cent, R.B.C. 5·47 m./c.mm., W.B.C. 10,950/c.mm., polymorphs 60 per cent, lymphocytes 35 per cent, eosinophils 5 per cent. Bleeding and clotting time normal. Blood Group O. Sputum for A.F.B. negative.

He was put on general lines of treatment without any antibiotics, as none seemed warranted. On 15-4-1955 segmental resection of the right lower lobe was performed. The operation notes run thus:

There was a cystic involved segment of the right lower lobe (posterolateral). There was an artery to this cystic segment from the aorta beneath the diaphragm. This artery was ligated and severed. The cystic segment was removed by blunt dissection. There was an artery to this segment and numerous communicating veins which drained into the pulmonary vein, and an artery from the main pulmonary artery. There was very little bleeding from the raw surface. The bronchus was closed with silk and the wound closed in the usual manner. On cutting open the resected specimen several cystic spaces were seen containing inspissated mucus which on smear examination showed no A.F.B., and a very few inflammatory cells. There was considerable fibrosis and no true alveolar structure was seen. The overlying pleura was thickened and adherent.

Postoperatively he was kept on achromycin capsules for about 15 days. He made an uneventful recovery, and was discharged on 9-5-1955. Postoperative x-rays revealed the usual postoperative pleural reaction (Fig. 2, *vide* Plate) but just prior to discharge this reaction had cleared up. The exaggeration of the bronchovascular markings noted previously throughout the lung persisted but no localised infiltration was seen.

Histology—Both the sections show more or less similar appearances. The wall of the cyst is lined by a layer of tall columnar epithelium which shows stratification at a few places. The subepithelial tissue is formed by bundles of collagen fibres and a few bundles of smooth muscle fibres. At a few places the wall of the cyst shows chronic inflammatory cell infiltration. Diagnosis—Congenital cyst of the lung. The artery in the section shows endarteritis (Fig. 3, *vide* Plate).

Discussion

Most of the theoretical considerations dealing with the embryology and pathogenesis of intralobar sequestration have already been covered in the introduction. It remains to be seen how far our case conforms to the classical descriptions.

Reference to Table 1 will conclusively demonstrate that ours was not a case of extralobar sequestration. Having established that, there is not much more we can postulate as lack of knowledge at the time of operation prevented us from carrying out studies like the lipiodol injection of the anomalous vasculature in the resected specimen, and a detailed examination of the artery itself and of the 'conducting' and 'functioning' components of Bruwer *et al* (1954).

Pathologically our specimen falls into Pryce's group 2, viz., a polycystic mass. The anomalous artery arose from the aorta below the diaphragm and probably conformed to the third category of anomalous arteries (Editorial, *J.A.M.A.*, 1954).

The classification described three types of anomalous arterial distribution: (1) abnormal artery to normally connected lung, (2) abnormal artery to sequestration mass and adjacent normal lung and (3) abnormal artery confined to the sequestered mass.

As far as the clinical aspect is concerned comparing our case with the description in medical literature, we noted several points of similarity and some dissonance. These have been set out in Table 2.

TABLE 2—SHOWING COMPARATIVE CHARACTERISTICS OF A CLASSICAL PICTURE AND THE PRESENT CASE

Classical picture	Present case
The patient is a child	The patient was a child.
Clinical course consists of bouts of fever, cough with expectoration. Foetor rare, sputum little	The clinical course was similar to that in the classical picture.
Clubbing of nails absent	Clubbing of nails absent.
Mediastinal shift absent	Mediastinal shift absent.
Radiologically when a communication is present fluid levels are seen in cysts	Radiologically fluid levels were seen in cystic spaces.
Bronchography shows no entry of oil into the cystic areas. Adjacent bronchial tree *may sometimes show bronchiectasis*	Bronchography showed no entry of oil into the cystic area. *No bronchiectasis* in the adjacent lung.
Bronchoscopy shows as apparently normal bronchial tree.	Bronchoscopy showed a normal bronchial tree.
Lesion lies in the posterior segment	Lesion lay in the posterior basic segment. Part of the lateral segment seemed also involved, though this could not be shown clearly.
Lesion usually on *left side*	Lesion lay on the *right side.*
Associated congenital anomalies of other structures hardly ever present	No other congenital defects were found.
The anomalous artery is a very large vessel *almost the size of the aorta*	The anomalous artery was the *size of the common carotid.*

CONCLUSION

In conclusion it must be reiterated that with further advancement of thoracic surgery, we should anticipate the exposition of more cases of intralobar bronchopulmonary sequestration. Unless we foster a high index of suspicion, we are going to overlook the diagnosis with serious results if we persist in medical management and with equally catastrophic sequels if we undertake surgery without being aware of the presence of the anomalous artery. In every case a pre-operative bronchogram is mandatory to assess how much bronchiectasis exists in the supposedly normal contiguous lung segments, so that adequate resection is planned. In the majority of cases it should be possible to establish a correct pre-operative diagnosis.

SUMMARY

A review of the literature on intralobar bronchopulmonary sequestration is given and a case reported.

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MANAGEMENT OF STATUS ASTHMATICUS AND CHRONIC ASTHMA WITH HORMONES

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It has been amply confirmed by various workers that bronchial asthma in all its phases can be controlled by the judicious use of hormones including adrenocorticotropic hormone, cortisone, hydrocortisone and the recent ones like prednisone and prednisolone. Almost all the workers agree that relief and its maintenance under the effect of these hormones is outstanding, though in all studies some cases of failure and partial response have been encountered. Reports of deaths while under this therapy are also not lacking (Savidge and Brockbank, 1954) and in the opinion of these authors cortisone cannot be completely exonerated from some responsibility for such deaths. To what extent this view is tenable, only further trials can show. The comparative value of each member of the above group has also been assessed (Schwartz, 1955; Gelfaud, 1953; Skaggs *et al*, 1955) as also their side effects and other complications (Wefford, 1953). Their use in ambulatory cases of chronic asthma has also been studied.

Experience of the use of ACTH in status asthmaticus has been reported by Aber *et al* (1954). Whatever the mechanism of action of these hormones may be there is no doubt that the clinical relief following hormone therapy is definite and at times dramatic. While this aspect of their action is being stressed, emphasis is also laid on the fact that their administration does lead to suppression of the adrenal functions and break-up of immunological defence, besides of course some other classical side-effects. Since the exact status of these complex body processes in a particular individual at the time of initiation of therapy cannot be established, the extent to which disturbances may be produced cannot be predicted. It is thus essential that the physician be on his guard and the patient effectively protected against adrenal suppression and infections.

The incidence of allergic diseases particularly of the nasorespiratory tract in the Simla Hills is very high and to date no effort has been made to assess the factors responsible for them. In hospitals it has been seen that a large number of cases seek admission with the onset of the rainy season and their number continues to swell uptil November, with a gradual decline towards the end of winter. A very large section of these cases consists of those suffering from chronic spasmodic asthma, some of which are very intractable and usually present in the hospital in advanced status asthmaticus.

The purpose of this study was to gauge the effect of ACTH in such cases of status asthmaticus who had proved refractory to all other antispasmodics and to assess the effect of cortisone and prednisolone in controlling chronic asthma and preventing relapses. No investigation as to the allergen responsible in individual cases or detailed respiratory physiological studies could be carried out for want of facilities. However, exhaustive clinical assessment was made and only those cases who had proved refractory to the use of other antispasmodics including adrenaline, ephedrine, aminophylline and antihistaminic agents, etc. were chosen for the hormonotherapy.

This group is a small one, but the results obtained have been so gratifying that it is hoped that the study would pave a way for more detailed investigations in those parts of our country where allergic disorders range high in incidence.

Materials and Method

The case material consisted of hospital patients derived from the private, general wards and the

Table 1—Showing Schedules of Treatment Followed

Schedule		No. of cases
	(A) STATUS ASTHMATICUS ...	10
First	Intravenous ACTH (aqueous) 20 units diluted in 200 c.c. of 5 per cent glucose in distilled water by drip method, 20-25 drops per minute ...	2
Second	Intramuscular ACTH (aqueous) 20 units injected at 6-hourly intervals (80 units in 24 hours)	8
	Both the above groups after the gradual withdrawal of ACTH were placed on the schedule as under B.	
	(B) CHRONIC ASTHMA ...	15
First	Oral prednisolone	11
	1st three days 5 mg. 4 times a day	
	Further 4 weeks 5 mg. 3 times a day	
	Next 4 weeks 5 mg. 2 times a day	
	Next 2 weeks 7½mg. a day	
	Maintenance dose 5 mg. a day	
Second	Cortisone tablets	4
	1st three days 25 mg. 4 times a day	
	Next 2 weeks 25 mg. 3 times a day	
	Further 4 weeks 25 mg. 2 times a day	
	Maintenance dose 25 mg. a day	

TABLE 2—SHOWING THE CLINICAL FEATURES AND LABORATORY FINDINGS

Sl. No.	Name	Age Sex	Duration of asthma in years	Duration of status asthmaticus in days	Presenting symptoms	Ortho-pnoea	Cyanosis	Rhonchi	B.P. in mm. Hg	Emphy-sema	WBC count	X-ray	Type of asthma
1	S.K.D.	50 M	15	8	Extreme dyspnoea, inanition, semicomatosed.	+++	++	+++	85/60	++	WBC 5100, P70 L24, M3, E3	Emphysema. Bronchial markings ++	Allergic
2	H.K.S.	36 F	15	6	do.	+++	+	+++	90/50	++	WBC 7800, P72, L22, M1, E5	do.	Allergic & psychological
3	S.R.	29 F	3	5	Severe dyspnoea, extreme inanition.	++	+	++	95/70	+	WBC 6400. P65, L30, M3, E2	do.	do.
4	M.V.	36 F	5	2	Severe dyspnoea, semicomatosed.	+++	++	+++	100/80	++	WBC 16000, P87, L13	do.	Infective
5	M.B.R.	28 F	5	10	Extreme dyspnoea, coma.	++++	+++	+++	Unrecorded	++	WBC 7800, P61, L35, M1, E3	do.	Allergic
6	M.B.	40 F	4	6	Severe dyspnoea, weakness.	++	+	+++	100/80	++	WBC 10000, P84, L13, E3	Thickened pleura on left side. Hilum ++	Allergic & infective
7	K.N.K.	30 M	1/6	3	do.	++	—	++	120/82	—	WBC 12100, P74, L16, M1, E9	No abnormality	do.
8	K.K.B.	32 M	7	3	Severe dyspnoea.	+++	+	+++	115/72	++	WBC 7100, P70, L22, M2, E6	Emphysema	Allergic
9	K.R.S.	40 M	3	2	do.	+++	—	+++	124/76	+	WBC 10300, P64, L31, M2, E3	do.	Infective
10	D.P.N.	41 M	5	3	do.	+++	—	++	120/72	++	WBC 5400, P62, L31, M2, E5	do.	Allergic
11	K.S.	40 M	1	—	do.	+++	—	+++	122/76	—	WBC 9600, P54, L40, M1, E5	No abnormality	do.
12	R.D.	40 M	2	—	Severe dyspnoea, weakness.	+++	+	+++	106/74	++	WBC 7800, P48, L44, M1, E7	Emphysema Bronchial markings	do.
13	M.S.	18 F	1	—	Repeated attacks of mild dyspnoea.	+	—	+	110/70	—	WBC 7400, P64, L30, M2, E4	No abnormality	do.
14	L.R.C.	34 F	1-3/4	—	do.	++	—	+	116/70	+	WBC 8500, P66, L30, M1, E4	Emphysema +	do.
15	M.V.*	32 F	½	—	do.	++	—	++	110/78	+	WBC 8300, P56, L37, M3, E4	do.	do.

* Only case in which family history of allergy was positive. P—polymorphs %, L—lymphocytes %, M—monocytes %, E—eosinophils %.

outpatients department. Out of the 15 cases treated, 10 presented in status asthmaticus and after the control of status asthmaticus these as well as the other five were all treated on either prednisolone or cortisone according to the schedules given in Table 1. In all the above cases, the clinical features have been summarised in Table 2.

The usual antispasmodics in adequate doses had failed to relieve the status asthmaticus, and proved of little avail in the spasmodic attacks also.

During this period general treatment including avoidance of possible triggers, good nourishing diet and symptomatic attention were adopted in each case. No other antispasmodic or antihistaminic drugs were used in any of these cases. In all cases blood pressure was recorded daily ; fasting urine was examined for glycosuria every alternate day. In addition, cases on cortisone were put on salt-free diet and were given potassium chloride 10 grains in capsule thrice daily. All the cases were covered by intramuscular strepto-penicillin bi-weekly except in one case who was protected by streptomycin alone in view of the past history of pleurisy.

Clinical Analysis

A reference to Table 2 will show that out of ten cases of status asthmaticus, 5 were males and 5 were females. The age varied between 28 and 50 years. The duration of status asthmaticus in which the patients presented was between 1 and 10 days. All the cases showed severe orthopnoea and restlessness. Seven of the patients were cyanosed from a mild to a moderate degree. Four of these were in a semi-comatose condition. All but two showed well marked emphysema. The laboratory examination revealed eosinophilic counts between 0 and 9 per cent. Radiology confirmed emphysema in eight of the cases with prominent bronchial markings.

Results of Therapy

First group (10 cases of status asthmaticus)—When placed on the therapy as per schedules mentioned in Table 1, the patients receiving intravenous ACTH took about two hours for the disappearance of their orthopnoea. Those administered ACTH intramuscularly took between 4 and 8 hours to break the status asthmaticus. In both these groups B.P. rose rapidly with the disappearance of the evidence of collapse and restoration of consciousness. Cyanosis took about 24 hours to disappear except in one case where it persisted for two days. On the average the lung signs took between 3 and 5 days to clear up except in one case in which these signs did not clear up till the seventh day.

Second group (5 cases in an asthmatic attack plus the 10 recovered from status asthmaticus). A reference to Table 3 will show that this group consisted of 10 cases recovered from status asthmaticus and in addition 5 cases who presented in an asthmatic attack, and in whom other antispasmodics were not successful in relieving the attacks. Upto the time of this analysis the cases had been on hormone therapy for periods varying from 12 to 36 weeks. All the cases except three continued to receive maintenance dose of the hormone.

To assess the clinical response the cases were grouped under the following categories :

1. *Complete control*—In these cases the treatment right from its beginning was able to completely control the attacks and kept the patients free from any spasms during the period of study and all of them are continuing the maintenance dose of the drug.

2. *Partial control*—In these cases the patients were completely controlled while in the hospital but relapse occurred on going home, the attack in relapse was however very mild. The drug, while at home, had to be temporarily increased to control the attacks and subsequently the case kept free of symptoms.

3. *No control*—In these cases no difference in the attack was made by the use of hormones.

4. *Worsening*—In these cases the condition worsened and attacks became more marked after the institution of hormone therapy. Analysing the cases on the above criteria as may be seen from Table 4, twelve out of the fifteen (80 per cent) of the cases fall in group 1, i.e., those cases in whom the attacks were completely controlled. The remaining 3 cases (20 per cent) though initially fully controlled, while in hospital, relapsed on returning to the original circumstances of life at home. In these 3 cases the attacks were controlled by temporarily increasing the dose of the hormone given. There is no doubt that in this group, the patients complained of minimal symptoms, particularly on physical and emotional stress, but the spasmodic attacks were fully controlled. There was no case in our series which belonged to group 3 or 4, i.e., who failed to respond or actually worsened on exhibition of the drugs. The maintenance dose has however to be continued for long period. Comparing the results of various schedules of therapy, the following observations were made :

1. In status asthmaticus, dramatic relief was obtained following the intravenous schedule of

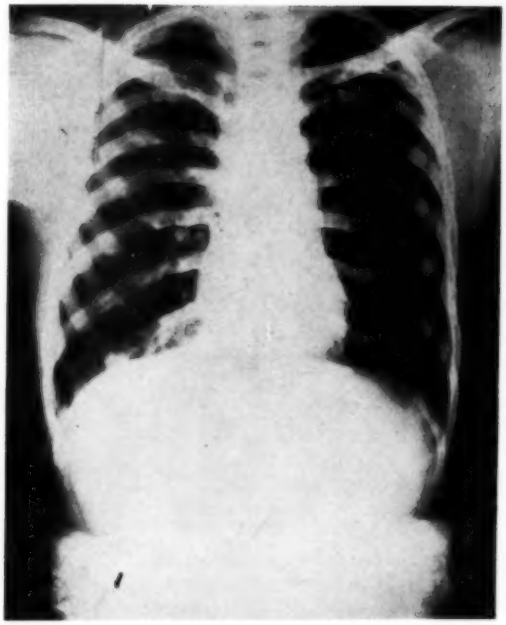

Fig. 1—X-ray appearance of lungs before operation. Right base shows cystic spaces.

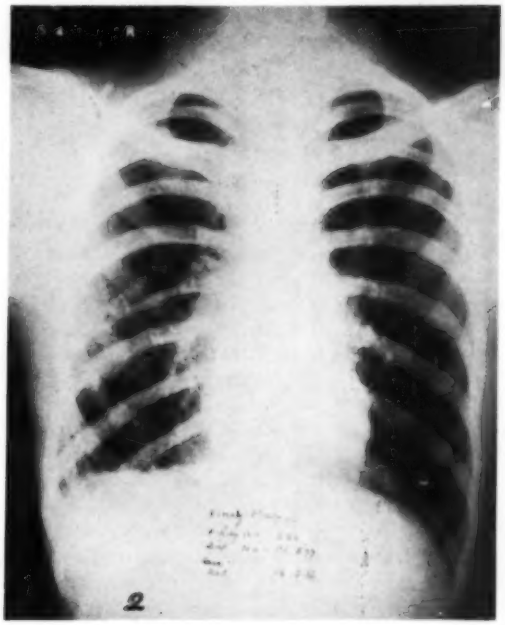

Fig. 2—X-ray appearance of the lungs after operation.

Fig. 3—Showing endarteritis of the pulmonary artery.

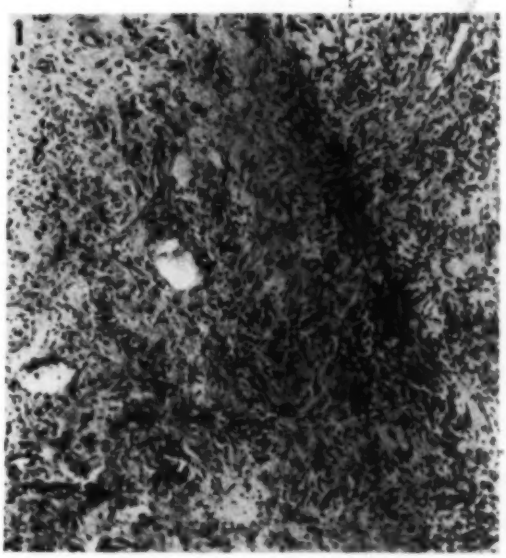

Fig. 1—Low power view of the tumour. (E. & H. × 80).

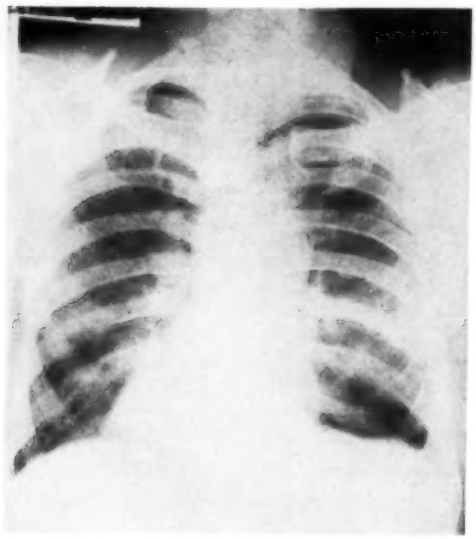

Fig. 1—Skiagram showing dextrocardia and increased lung markings at the left hilum.

Fig. 2—Small frontal sinuses and evidence of maxillary sinusitis.

Fig. 3—Bronchogram. Right anterior oblique view to show bronchiectasis of the branches of the left bronchus.

Fig. 4—Resected specimen of lung showing marked bronchiectasis.

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TABLE 3—SHOWING THERAPY AND ITS RESULTS IN STATUS ASTHMATICUS

Sl. No.	Name	Management during the attack		Response				Lung signs disappearance (days)
		Drugs used	Other management	Disappearance of dyspnoea (hours)	B.P. (mm. Hg) Initial	B.P. (mm. Hg) Final	Cyanosis disappearance	
1.	S.K.D.	20 units of ACTH in 200 c.c. of 5% glucose intravenous slowly in 2½ hrs.	Oxygen for one hour	2½	85/60	100/60	1 day	4
2.	H.K.S.	—do—	—do—	2	90/50	115/70	—do—	3
3.	S.R.	20 units of aqueous ACTH intramuscular six hourly	—do—	6	95/70	100/70	—do—	3
4.	M.V.	—do—	—do—	4	100/80	115/80	—do—	4
5.	M.V.R.	—do—	Oxygen for ½ an hr. 200 c.c. of glucose with vitamin C 500 mg. and vitamin B_1 100 mg.	4	Could not be recorded	100/70	2 days	5
6.	M.B.	—do—	Oxygen for ½ an hour only	8	110/80	132/100	1 day	7
7.	K.N.K.	—do—	—	8	120/82	122/80	No cyanosis	3
8.	K.K.B.	—do—	—	6	115/72	124/72	1 day	4
9.	K.R.S.	—do—	—	4	124/76	124/76	No cyanosis	3
10.	D.P.N.	—do—	—	7	120/72	122/72	—do—	5

TABLE 4—SHOWING THERAPY AND RESULTS IN CHRONIC ASTHMATIC ATTACKS

Sl. No.	Name	Drugs used				Response	
		Cortisone duration (weeks)	Total dosage (g.)	Prednisolone duration (weeks)	Total dosage	Complete control	Partial control
1	S.K.D.	16	5·5	—	—	+	
2	S.R.	12	4·2	—	—		+
3	K.R.S.	36	8·87	—	—		+
4	H.K.S.	—	—	28	1·52 g.	+	
5	M.V.	—	—	24	1·22 g.	+	
6	M.B.R.	—	—	18	1 g.	+	
7	M.B.	—	—	21	1·1 g.	+	
8	K.K.B.	—	—	21	1·1 g.	+	
9	K.N.K.	—	—	21	1·2 g.	+	
10	D.P.N.	—	—	28	1·5 g.	+	
11	K.S.	—	—	15	865 mg.	+	
12	R.D.	12	2·77	—	—		+
13	M.S.	—	—	13	795 mg.	+	
14	M.V. (2)	—	—	12	538 mg.	+	
15	L.R.C.	—	—	18	1·02 g.	+	
						12	3

No case of failure of response occurred.

aqueous ACTH. The response in patients given intramuscular hormone was comparatively slower.

2. In cases of chronic asthma receiving prednisolone in doses almost ⅛th of cortisone, showed almost equal clinical control.

3. In cases on prednisolone, no salt restriction or additional potassium appeared to be necessary.

4. In status asthmaticus, the rise in blood pressure was very salutary to the patient presenting in collapse but in no case severe hypertension, glycosuria or haemorrhages occurred.

5. Smaller dosage schedules as employed in this group appear to be quite adequate.

Side Effects

As appears from Table 5 the incidence of side effects was, on the whole, minimal. No side effects were encountered in cases of status asthmaticus who were put on ACTH, but the duration was too short in these cases. Cortisone cases showed more side effects than those receiving prednisolone, though in the latter cases epigastric symptoms were more and so also a tendency to insomnia. But none of these were such as to warrant an interruption of therapy.

Table 5—Showing the Side-Effects of Hormone Therapy

Side-effects	Cases on cortisone with salt restriction and additional potassium	Cases on prednisolone with no salt restriction and no additional potassium
Increase in weight		
Marked (++) ...	All ++	
Slight (+) ...		All +
Mooning of face		
Marked (++) ...	All ++	
Mild (+) ...		All +
Hypertension (mild)	2	1
Glycosuria ...	1	Nil
Epigastric discomfort	2	2
Hirsutism ...	4	1
Infections ...	1	1
Dizziness ...	1	Nil
Tachycardia ...	Nil	1
Insomnia ...	Nil	2

N.B.—None of the side-effects were seen in cases of status asthmaticus put on ACTH.

Discussion

Reports of the gratifying results of cortisone in all allergic disorders have appeared ever since its discovery. In chronic asthma, trials of the drug have been made since 1952 and a very large number of reports has been published on the control of the condition with cortisone.

Schwartz (1955) tried metacortandracine and metacortandralone on two of his patients, one suffering from chronic bronchial asthma with diabetes mellitus and the other with nasal polypus. He made the interesting observations that these drugs were 3 to 4 times more potent than cortisone and 2-3 times more potent than hydrocortisone.

In a symposium on the use of these drugs in asthma, Brown (1954) observed that those cases of asthma who were due to atopy got rapid relief with cortisone as compared to those whose asthma was due to infection. He also observed that combined use of prednisone and ACTH reduced the side-effects. As already stated these results were confirmed by detailed study carried out by Carey *et al* (1950).

In status asthmaticus the intravenous use of ACTH had also been advocated (Aber *et al*, 1954 ; and Braur *et al*, 1953) ; and physiological studies on pulmonary functions conducted by Barach (1955) showed very gratifying results.

Taking the other side of the picture the main question that arises is whether this therapy can prove harmful. Savidge and Brockbank (1954) while carrying out a well controlled study observed two deaths—one in a case of perennial asthma who recurrently passed into status asthmaticus which in spite of increasing the maintenance dose of cortisone could not be controlled and took the patient away ; the other almost similar but less severe case who also died in status asthmaticus and in whom the double dose of the hormone could not be administered in time. At necropsy the death appeared to be due to asphyxia due to bronchial obstruction by plugs of tenacious sputum. Neither any pulmonary infarction nor any sign of right sided heart failure could be found. However, the adrenal glands were small from which it was presumed that the stress of the terminal illness could not be effectively met by suppressed adrenals. The authors confess that both these cases had considerably worsened before treatment and in both of them suppression of asthma was never fully achieved and the spasms tended to break through even the increased maintenance dose. In spite of this however, they felt that cortisone could not be completely exonerated in contributing towards the fatal issues.

They have analysed 11 deaths that have been reported in the literature out of many series of trials in which a very large number of patients have been treated by various workers.

To what extent hormones can be directly implicated with these deaths is still very doubtful

because most of the deaths have been in intractable cases, complicated by persistent status asthmaticus or other complications. Notwithstanding the above there is no doubt that a large number of workers reported on the outstanding effect of the hormones in chronic spasmodic asthma, and as far as the small number of cases reported in this series we have not encountered any such grave happening in any of our cases.

As will appear from the results tabulated our cases have been on adequate doses of these hormones for between 12-36 weeks and though the number of cases is only fifteen, yet they include all forms of asthma and as many as ten of rather severe asthmatic state. In none of them have any considerable untoward results been seen. As to the side effects, our experience is that prednisolone is far superior to cortisone, probably because of the very small maintenance dose required. This study confirms the experience of others in the dramatic control of status asthmaticus particularly by the use of intravenous ACTH. All our cases are now ambulatory with maintenance dose and in this behalf we agree with the findings of Turiaf and Chabot (1952). It is not possible to comment on withdrawal effects of the maintenance dose but it may be stated that cases, included in this series are only those in whom all other drugs had failed to keep the attack under control and the effect is achieved by prolonged maintenance dose particularly with negligible side effects, appear to be quite satisfactory in our group of cases. In our observations out of the fifteen cases, 12 are still continuing on maintenance doses and in the three in whom the drug has been gradually withdrawn upto date persistent relief has been experienced. In the remaining 12, attempts at withdrawal of the maintenance dose leads to minimal symptoms and therefore minimal therapy is being maintained. More trials on more elaborate basis in more combinations would perhaps be required before a definite statement on final relief of these cases can be made. However it can be safely concluded that though not a cure, this therapy achieves effective suppression with almost complete clinical relief even in those cases who are refractory to all other drugs.

Summary

The effect of intravenous and intramuscular ACTH has been studied in ten cases of advanced status asthmaticus resistant to other antispasmodics. Remarkable effect with rapid amelioration has been noted. The authors conclude that the measure is life saving in some of the cases. Their experience places intravenous use as superior to intramuscular administration in treating status asthmaticus.

The effect of prolonged prednisolone and cortisone therapy on chronic asthmatic attacks has been observed in fifteen cases for a period extending upto over 36 weeks. Authors report complete control in 80 per cent and partial control in 20 per cent of the cases maintained on a maintenance dose. Their experience places prednisolone superior to cortisone in the long range therapy.

No death, no case of worsening, complete failure or of severe side effects has been encountered in this small series.

The literature on the point has been briefly reviewed.

Acknowledgments

We are thankful to Dr. Sant Ram Vaidya, Pathologist, and to Dr. M. L. Ahuja, Radiologist, for their cooperation during these studies. Our thanks are also due to Dr. B. M. Bharadwaj for his help in scrutinising the article.

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Addendum

Since the time of writing this article 10 more patients, refactory to ordinary antipasmodics, have been treated for chronic asthma with prednisolone in the dosage schedule as given in the text. Complete clinical relief was experienced by nine of these cases. One case of long standing severe asthma with frequent episodes of status asthmaticus failed to respond and the drug had to be withdrawn due to severe insomnia and anxiety tension noted in this case. With the addition of these ten cases our total experience of the application of hormones in cases of asthma refractory to other drugs comes to 25.

Total number of resistant cases treated	25
Complete clinical relief observed by ...	21 cases
(a) Patients still on maintenance dose ...	17
(b) Patients quiescent after withdrawal of maintenance dose	4
Partial control	3
Failure	1
Worsening or death	Nil

BYSSINOSIS*

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INTRODUCTION

In industrial medicine many occupational dust diseases have been described under the term pneumokoniosis (*pneumon*—lung ; *konis*—dust). Byssinosis is a condition usually found in cotton mill workers due to inhalation of cotton dust over a number of years. The disease is described to be common in strippers and carders in a textile mill but is not uncommon in weavers.

It was first reported by Jackson in 1818 who observed that those who worked in cotton industry, particularly cardroom workers, suffered from a characteristic respiratory disease resembling chronic bronchitis and asthma. However much investigational work was not done till 1930's. An outbreak of the disease was reported in some 25-30 workers when carding machines were cleaned with compressed air producing a fog of cotton fibres. The early symptoms were usually due to allergy and were not incapacitating, but prolonged exposure for a number of years gradually incapacitated the worker leading to a clinical and pathological condition of pulmonary emphysema and possibly fibrosis which eventually led to right-sided cardiac failure.

Usually there is no pulmonary fibrosis, only in well developed cases there are evidences of pulmonary emphysema, and because of this, this disease is not included in 'pneumokoniosis' which means fibrosis of the lungs due to inhalation of dust and also not governed by the laws relating to pneumokoniosis for compensation purposes ; but in U.K. there is a special byssinosis regulations for compensation to workers working more than 20 years. It is, however, an occupational disease.

AETIOLOGY

Though not universally accepted, the predisposing causes of the disease seem to be defective ventilation, bad hygienic conditions, poor diet and alcoholism all leading to a debilitated state with low resistance.

PATHOGENESIS

Pathogenesis is still a matter of debate. The toxic agent in cotton dust may be :

(a) The protein fraction of card room dust which has been shown to be capable of producing irritation and inflammation of the upper respiratory tract leading finally to chronic bronchitis, both in animals and in men. Also the characteristic course of the disease is suggestive of an acquired allergic hypersensitivity, and there is some confirmation of this view in the finding of positive cutaneous reaction to the proteins in affected persons, but only rarely in unaffected persons.

(b) Other factors suggested are, substances resembling histamines and moulds ; but histamine-like substances similar to those in cardroom dust have, however, been found in other dusts not causing similar symptoms alone. So possibly these are toxic when in combination. Inorganic components have not been blamed.

In almost all departments of textile mills a good percentage of humidity is maintained for proper working of the yarn (Table 1).

Temperature variation and humidity may play a part as a predisposing cause.

TABLE 1—SHOWING THE HUMIDITY AND TEMPERATURE MAINTAINED IN DIFFERENT DEPARTMENTS

	Humidity %	Temperature in °F
Blowroom ...	50—55	80—70
Carding room ...	55—65	85—74
Spinning room ...	65—70	90—80
Weaving room ...	80—90	95—91

In U. K. cotton arrives in cotton mills in tightly compressed bales (from India, Egypt and U.S.A.) which also contain much foreign material such as particles of leaf and seed coat, cotton hairs, fragments of moulds and fine sand. The raw cotton, therefore, has to be first cleaned, and the tightly compressed cotton is pulled off in layers and hand-fed into the machine called 'hopper bale opener'. It then passes into the blowing room where a series of machines by means of beating actions and currents of compressed air free it from most of the impurities. All these machines are usually enclosed in dust-proof covers but the machines have to be cleaned.

* Read at the monthly meeting of Medical Officers in the office of the Deputy Director of Medical and Health Services, (E.S.I.) U.P., Kanpur, March, 1956.

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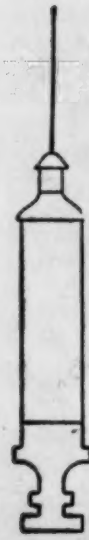

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This is a particularly dusty job and the workers have to suitably clothe themselves and wear inspirators. The clean cotton coming out of the blowing room passes to the carding engines and it is principally the strippers and grinders in charge of these carding engines who suffer from this disease.

Usually each engine is cleaned 4 times daily by a vacuum process and twice weekly it is brush-stripped (because the vacuum cleaning fails to clean sufficiently deeply).

The evidence is strong that the dust liberated by the process in the immediate vicinity of the carding engine contains the injurious dust producing byssinosis.

Slivers are made here from laps of cotton and they are passed on to the spinning department. The size of cotton fibres is still smaller in this department and yarn making starts here. Finally the yarn after a sizing process goes to the weaving department. The maximum to and fro motions are seen in this department. The cotton fibres blown in this department are probably of the smallest size and because of the sizing material along with them they appear to be easily adhesive to the mucous membrane of the respiratory tract than the fibres of other departments.

The pathological picture of chronic interstitial bronchitis is seen in early stages. The cotton dust fibres are inhaled and deposited in the squamous epithelium of the lung alveoli. From here they are phagocytosed and carried by the lymphatics to the interstitial tissues of the lung. Minor inflammatory foreign body reaction is produced. The elasticity of the lung parenchyma is lost leading to emphysema, which causes impairment of ventilation and thus dyspnoea. At a later stage emphysema and right-sided cardiac failure occur. The degree of impairment is directly related to the years of continuous exposure, the concentration of the dust inhaled and general resistance of the worker.

Macroscopically, as was observed (Hollander, 1953) in a necropsy case of byssinosis, the lung was voluminous with areas of consolidation and scattered haemorrhagic spots. Bronchial and hilar lymph nodes were enlarged. The histopathological changes noted by him were marked thickening and fibrosis of the alveolar walls, with epithelisation in areas of extensive fibrosis.

Clinical Features

This history of prolonged exposure to cotton dust is always available. The duration is usually 10-20 years.

The symptom of 'not being well' as the worker goes to work appears to be the earliest symptom that could be observed in these cases. The other earlier symptoms described are those similar to allergic rhinitis with sneezing, dry and irritating cough, and tight feeling in the chest, lasting for 1 or 2 days at first, but returns after a short absence from work, e.g., 'weekend'. As these symptoms are only produced for a short time on resuming work after a rest day and then subside till in the next week after a rest day, allergic phenomenon appears to play its role in the beginning till some organic changes in the lung parenchyma take place. Symptomatically, therefore, these cases can be divided to belong to 3 stages. In the first stage there is breathlessness only after a rest day, in the second stage the breathlessness persists on all days of the week and in the third stage because of emphysema, the breathlessness persists throughout, irrespective of rest or working days.

Clinically in the first stage no signs can be detected in the lungs. The breathing capacity is usual and unless accompanied by some superimposed secondary infection, which is a common feature in many of these cases no adventitious sounds are heard. In the second stage of the disease there is slight diminution in the breath sounds, the bases being more dull. In the third stage due to the emphysematous changes increased resonance is characteristic along with rhonchi and crepitations. There is however no water-tight compartment for these stages as one stage can easily merge into the other.

There are no other constitutional symptoms except a low grade fever which many become immune to in a few weeks or months. The fever is usually confined to Monday morning and is called 'Monday morning fever', 'mill-fever' or 'factory fever'. In the later stages after about 10-20 years of the initial sickness the fever reappears gradually, the cough becomes dry and severe and the symptoms appear every day. The sputum is scanty and tenacious in nature. Early fatigue and low tolerance to work develop until finally emphysema develops.

X-ray examination—X-ray examination of the chest is of little help in the diagnosis of byssinosis. The x-ray picture may be of some help along with the clinical features and occupational history. The presence of nodular or miliary shadows distributed evenly over both lungs must be considered as non-specific. The x-ray appearance of all the pulmonary conditions due to occupational dust gives a basic pattern that the dust aggregates mainly in the peribronchial and periarterial lymph nodes and

lymph channels (McLaughlin, 1952). Thus the main feature in all the roentgenograms (as seen in this series also) is prominence of the hilar shadows and bronchovascular markings.

Laboratory findings—Almost all of these cases investigated for tuberculous infection showed no acidfast bacilli on repeated sputum examinations.

Blood sedimentation rate in some of the cases varied within normal limits.

R.B.C. count and Hb. percentage in some cases revealed a slight degree of anaemia.

W.B.C. count in all cases showed an inappreciable degree of leucocytosis. One point which was striking was that all these cases had slightly raised eosinophilic count from 5 to 10 per cent as compared to the normal 1 to 3 per cent. This is probably in favour of the allergic phenomenon.

Prognosis

The disease has a prolonged course. The early symptoms begin after several years of cotton dust inhalation. The emphysematous changes in the lung tissue take still longer time to develop when the vital capacity is very much diminished. Right-sided congestive cardiac failure ensues at the last stage usually ending fatally.

Treatment

The prevention is the main treatment. In some persons the disease does not produce any effect, throughout their lifelong period, but in others the symptoms appear early. Personal factors play an important role. As soon as any symptom is observed, it is always advisable to shift a patient to some other non-dusty occupation.

The treatment on general lines has been found to be of some benefit in these cases. Injections of calcium gluconate intravenously and an antispasmodic mixture with ephedrine have been beneficial. In those cases who have associated anaemia, the use of an iron preparation and sometimes cyanocobalamine injections give good results. For superimposed bacterial infection, sulpha drugs and antibiotics have been envisaged with benefit. Aminophylline because of its bronchodilatory effects has also been tried with benefit. As the early symptoms are attributed to allergic phenomenon anti-allergic drugs have been used in some of the cases, but without any appreciable difference in the condition. Arsenic preparations administered in some cases of non-specific eosinophilia have given relief.

Case Summaries

In the series under review 21 cases were observed and the incidence of the disease according to different departments of the mill was as follows:

Weaving department—13; carding department—7; spinning department—1; blow room—nil. Although the disease has been described to be more common in carders and spinners, the incidence was maximum in weavers in this series.

Out of the 20 cases, 19 had associated respiratory catarrh.

Details of the individual cases are given below:

Case 1—B.L., aged 33 years, male, working in the spinning department for about 10 years came with complaints of cough for 4-5 years, dyspnoea developing within 1-2 hours while working in the mill and weakness for 1 year. The illness started 4-5 years after his acceptance of the present occupation. He also complained of dry cough with scanty, thick sputum.

On examination he appeared healthy. Prolonged inspiration was the only abnormality.

Radiologically the lungs were clear.

B.S.R. was 3 mm. (Westergren); Hb. 84 per cent; R.B.C. 4·13 million/c.mm.; W.B.C. 6200/c.mm, polymorphs 60 per cent, lymphocytes 34 per cent and eosinophils 6 per cent.

The patient was kept on the general line of treatment and could resume work without any difficulty. This was an early case manifesting the first stage of the disease where only symptoms were present.

Case 2—B., aged 37 years, male, working in the carding department for 6 years came with complaints of common cold off and on, cough with occasional expectoration for 4 years and dyspnoea while at work for one year. The onset of illness was gradual. He had attacks of sneezing often in the factory while working on the carding machine. For the last one year he had a feeling of discomfort in breathing when working after a rest day. He was better on other days and normal when at home.

On examination he was of good build. Breath sounds were harsh on both sides. There were no adventitious sounds.

Radiologically bronchovascular markings were prominent.

W.B.C. 8600/c.mm., polymorphs 65 per cent, lymphocytes 28 per cent and eosinophils 7 per cent.

The patient was treated with 'antistine' for 7 days. Injections of calcium gluconate I.V., biweekly and an expectorant mixture gave him temporary relief.

Case 3—B., aged 60 years, male, of the carding department working for the last 20 years, had complaints of cough with expectoration and weakness for 4 years. He gave a history of haemoptysis 3 years back. He was dyspnoeic while working in the mill for 1 year only in the second half of his working period. On resuming work he was not dyspnoeic and worked without much difficulty. After half time when he used to resume work again he felt dyspnoeic and it was difficult for him to work unless he took rest for 4-5 minutes. He complained for 'Monday morning sickness' and when duty

was changed after 15 days. The trouble was more in the night shift.

On examination he was of average build. The lungs showed occasional rales with prolonged inspirations.

Radiologically hilar shadows and bronchovascular markings were prominent showing a picture of bronchitis.

B.S.R. was 5 mm./1st hour (Westergren). W.B.C. 7000/c.mm., polymorphs 70 per cent and lymphocytes 30 per cent.

The patient was kept on calcium gluconate injections and had cod liver oil, iron mixture and a sedative cough mixture.

This case, initially a case of bronchitis, had superimposed byssinosis, as suggested by the occupational history.

CASE 4—B, aged 52 years, male, working in the weaving department for about 12 years, complained of cough and dyspnoea for the last 3 years and weakness for 2 years. He had to clean the floor of the mill where cotton dust accumulated. Breathlessness was present on all the week days from the very beginning during working hours only. Now for about 1 year he was breathless at home also, after slight exertion.

On examination he was of poor build with nutrition below average. Respiratory system showed a few wheezing rhonchi and harsh vesicular breathing. Slight tachycardia was present.

Radiologically lung fields were clear.

W.B.C. 7400/c.mm., polymorphs 55 per cent, lymphocytes 36 per cent and eosinophils 9 per cent.

The patient was treated symptomatically with expectorant mixture, injections of adrenalin, ephedrine and antistine when required which gave temporary relief. Calcium gluconate injections were also given bi-weekly with a little improvement.

CASE 5—J.P., aged 43 years, male, working in the weaving department for 9 years came with the complaints of cough with thick expectoration for 4½ years and dyspnoea while working in the mill for 1 year. The onset was gradual. The patient complained of dyspnoea in the beginning of the day's work after a few hours of exertion, for which he usually took rest for 10-15 minutes and then only he was fit for work till the evening. At the close of the day's work he had some shortness of breath again. He was well at home.

On examination he was of poor build. Vocal resonance was increased on both sides. On auscultation a few rhonchi were heard.

Radiologically bronchovascular markings were prominent.

B.S.R. was 30 mm./hour. W.B.C. 6000/c.mm., polymorphs 56 per cent, lymphocytes 40 per cent and eosinophils 4 per cent.

Treatment was given on general lines.

In this case also byssinosis was superimposed on bronchitis or both conditions coexisted.

CASE 6—B., aged 34 years, male, working in the carding department for a period of nearly 7 years came with complaints of cough for 4 years and dyspnoea while working after a rest day, for 2 years. The illness started with cough and thick expectoration 4 years back. For the last 2 years symptoms of dyspnoea developed. The breathlessness was felt on resuming work after a day's rest. On other working days he was better. He had practically no complaints when at home.

On examination he was found to be of a poor build, under-nourished and anaemic. Lungs did not show any abnormality.

Radiologically hilar and bronchovascular markings were prominent.

B.S.R. was 4 mm./hour (Westergren). W.B.C. was 6800/c.mm., polymorphs 65 per cent, lymphocytes 30 per cent and eosinophils 5 per cent.

Treatment was given on general lines.

This was an early case of byssinosis and was associated with bronchitis.

CASE 7—B., aged 44 years, male, working in the weaving department for a period of about 23 years came with complaints of cough with thick expectoration for 6 years, dyspnoea at work for 3½ years, feverishness after week's rest day and myalgia of the whole body for 2 years. He felt dyspnoeic in the early hours of the day's work for 2-3 hours and was better afterwards on all working days. He was well at home. He had associated symptoms of bronchitis also.

On examination he had a poor build, was undernourished and slightly anaemic. Lungs showed occasional coarse crepitations.

Radiologically lungs did not show any abnormality.

B.S.R. was 17 mm./hour (Westergren), R.B.C. 4·15 million/c.mm., Hb. 12 g./per cent, W.B.C. 7200/c.mm., polymorphs 71 per cent, lymphocytes 25 per cent and eosinophils 4 per cent.

Treatment was given on general lines with temporary relief.

CASE 8—S., aged 25 years, male, of the carding department working for a period of 16 years with the complaints of recurrent attacks of coryza for 10 years, cough with expectoration for 5 years and dyspnoea while at work for 4 years. He felt dyspnoeic on resuming work in the mill. He worked without much difficulty for the first few hours but gradually developed dyspnoea towards the end of the day's work. He worked with better efficiency if he took rest for about 10-20 minutes after a few hours' work. He was dyspnoeic on all the working days but was well at home.

On examination he was a well built man with good nutrition. Respiratory system showed increased resonance on both sides and diminished breath sounds more towards bases.

Radiological examination was done twice and showed prominent hilar and bronchovascular markings.

B.S.R. was 4 mm./hour (Westergren). W.B.C. 8000/c.mm., polymorphs 67 per cent, lymphocytes 30 per cent and eosinophils 3 per cent.

Treatment was given on general lines. The respiratory symptoms were controlled by penicillin injections but symptoms of byssinosis continued.

CASE 9—S.L., aged 55 years, male, of the weaving department working for a period of 19 years came with the complaints of cough for 18 years, dyspnoea and breathlessness for 10 years and frequent attacks of asthma during the working hours. The onset of the

present symptoms started after a rest day on the following morning. The patient developed dyspnoea when at work for ½ to 1 hour. This subsided gradually and he did not feel any discomfort till the evening. This condition continued for 2-3 years. Later on he felt dyspnoea on week days also. This was for about 2 years. For the last 5-6 years he has developed dyspnoea throughout the day more during working hours and with very little relief when he took rest at home. It was about 1½ years when he was shifted from the weaving department to the store room and he has been much relieved by this change though not completely.

On examination he appeared a weakly built man with poor nutrition. He had a barrel-shaped chest with emphysema lung. Breath sounds were feeble and wheezing rhonchi were heard occasionally. Heart sounds showed increased intensity, there was tachycardia and the heart was dilated. The neck veins were visible. The blood pressure was 160/96 mm. of Hg.

Skiagram of the chest showed increased transparency of the lung fields with increased hilar and perihilar shadows.

W.B.C. 12,500/c.mm., polymorphs 84 per cent, lymphocytes 8 per cent, eosinophils 8 per cent. This was during an attack of bronchitis.

Treatment was given with adrenaline injections, ephedrine, asthma mixture and aminophylline tablets and injections. This was a fairly advanced case of byssinosis in which emphysematous changes had taken place with secondary right-sided cardiac failure.

CASE 10—M.L., aged 42 years, male, of the weaving department working for a period of 21 years came with the complaints of cough for 15 years, dyspnoea during working hours for 7 years and graduual development of weakness for 6 years. He suffered from breathlessness while at work about 7 years ago. The trouble started in the morning hours and subsided after 1-2 hours. After about two years, whenever he had dyspnoea during duty hours he was not relieved till he took rest for about 10-15 minutes and breathed fresh air. At present he has a feeling of suffocation at every 2-3 hours interval and cannot work unless he takes a rest of 15-20 minutes each time.

On examination he was of a poor build. Respiratory system showed increased resonance on both sides of the chest with feeble breath sounds. On auscultation wheezing rhonchi with occasional rales were heard.

Radiologically increased hilar shadows with few calcified glands and prominent bronchial markings were seen.

W.B.C. 8,000/c.mm., polymorphs 81 per cent, lymphocytes 14 per cent and eosinophils 5 per cent.

B.S.R. was 5 mm./hour (Westergren).

Treatment was given on general lines and gave temporary relief.

CASE 11—B.L., aged 49 years, male, working in the weaving department for a period of 21 years came with complaints of cough for about 15 years and dyspnoea during working hours for 1 year. He kept well for 5-6 years after taking up the occupation and the cough developed afterwards. At present the patient is dyspnoeic throughout the day's work all the days of the weak. He is better at home but as soon as he joins his duties he is unable to work. He has to take rest for a few minutes after every hour of work.

On examination his build was average but undernourished. Respiratory system showed increased resonance, diminished breath sounds with occasional wheezings, B.P. was 170/90 mm. of Hg.

Radiologically lungs showed prominent bronchovascular markings.

B.S.R. was 20 mm./hour (Westergren). W.B.C. 8600/c.mm., polymorphs 80 per cent, lymphocytes 16 per cent and eosinophils 4 per cent. He was treated for bronchitis. But symptoms of dyspnoea at work are still present.

CASE 12—B., aged 37 years, male, working in the weaving department for a period of 16 years came with the complaint of difficulty in breathing for 3 years and feeling of tightness of chest for the last 3 months. The patient is well at home but on work became dyspnoeic. About ½ to 1 hour after work he felt better. The dyspnoea was aggravated again towards the end of day's work. He was well by the time he reached home.

On examination he was of average build with fair nutrition. Chest examination showed increased resonance at bases and harsh vesicular breathing.

Radiological examination showed no abnormality.

B.S.R. was 6 mm./hour (Westergren). W.B.C. 6700/c.mm., polymorphs 52 per cent, lymphocytes 40 per cent, monocytes 1 per cent and eosinophils 7 per cent.

Routine treatment was given and there was temporary relief each time.

CASE 13—L.N., aged 37 years, male, working in the weaving department for a period of about 17 years came to the dispensary with complaints of cough for 10 years, dyspnoea at work after rest days for one year and gradual development of weakness for one year. He felt dyspnoeic in the mill only after rest days. When he resumed his work, he was well for the first 1-2 hours and developed breathlessness later, which increased gradually till the half time interval. On resuming work after half time he did not feel dyspnoeic and could work without difficulty towards the closing of the day's work.

On examination he was well built but of poor nutrition. Chest examination did not show any abnormality.

Radiologically lungs were normal except for prominent hilar and bronchovascular markings.

B.S.R. was 12 mm./hour (Westergren). W.B.C. 8600/c.mm., polymorphs 64 per cent, lymphocytes 29 per cent and eosinophils 7 per cent.

Treatment was given on general lines and the patient improved.

CASE 14—K., aged 50 years, male, working in the weaving department for a period of about 30 years came with complaints of cough for 13 years and difficulty in breathing for 4 years. The onset of illness began with common cold. He had difficulty in breathing all the seven days of the week when working in the mill. He was unable to work at a stretch for more than 2 hours. He had to take rest for 10-15 minutes. He felt better in open air and when at rest.

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On examination he was of average build with poor nutrition.

Chest examination showed harsh vesicular breathing with occasional rales.

Radiologically hilar and bronchovascular markings were prominent.

W.B.C. 6800/c.mm., polymorphs 70 per cent, lymphocytes 24 per cent and eosinophils 6 per cent.

He was treated on general lines with temporary improvement.

Case 15—B.D., aged 30 years, male, of the carding department working for a period of about 15 years came with complaints of cough for 4 years and difficulty in breathing during working hours for 1 year. The patient often attended the dispensary with cough for about 4 years but for the last 1 year he had difficulty in breathing towards the end of the day's work. He was quite well as soon as he was outside the mill.

On examination he was of good build with fair nutrition. Chest examination did not reveal any abnormality.

Radiologically lung fields were clear.

W.B.C. 8200/c.mm., polymorphs 67 per cent, lymphocytes 28 per cent and eosinophils 5 per cent.

Treatment was given on general lines with some improvement.

Case 16—B.D., aged 43 years, male, working in a weaving department for about 21 years came with complaints of cough with thick expectoration for 5 years and a feeling of tightness in the chest for 1½ years. When going to work he had a feeling of being unwell and chest tightness about an hour after resuming work. He was quite well outside the mill.

On examination there was no abnormality.

Radiologically hilar shadows and bronchovascular markings were prominent.

W.B.C. 8200/c.mm., polymorphs 63 per cent, lymphocytes 31 per cent and eosinophils 6 per cent.

Treatment was given on general lines with little improvement.

Case 17—A.G., aged 40 years, male, of the weaving department working for a period of about 13 years came with complaints of cough for 8 years and dyspnoea during working hours for 2 years. He had a few attacks of bronchitis in the past. He felt dyspnoeic on all working days of the week. He could only work with a pause of 10-15 minutes after every 2-3 hours. He was better at home.

On examination he was of average build with poor nutrition. Chest examination showed resonant note on both sides, with occasional rales at the lower zones.

Radiologically lungs were normal.

W.B.C. 7800/c.mm., polymorphs 70 per cent, lymphocytes 25 per cent and eosinophils 5 per cent.

The treatment was given on general lines with some improvement.

Case 18—R.D., aged 45 years, male, of the carding department working for a period of 17 years came with cough for 6 years and dyspnoea for 5-6 months. He was quite well at home, but had dyspnoea in the mill towards the end of the day's work.

On examination he was of poor build with poor nutrition. Chest examination showed harsh vesicular breathing.

Radiologically lungs were clear.

B.S.R. was 16 mm./hour (Westergren). W.B.C. 7200/c.mm., polymorphs 84 per cent, lymphocytes 12 per cent and eosinophils 4 per cent.

Treatment was given on general lines with satisfactory improvement.

Case 19—B., aged 42 years, male, working in the weaving department for a period of about 10 years, came with the complaints of cough for 4-5 years and dyspnoea in the mill for 1 year. Onset of symptoms began with common cold and later on he developed cough. His dyspnoea starting about an hour after resuming duty persisted till half time on all working days.

On examination he was a well built man with poor nutrition. Chest examination showed harsh vesicular breathing.

Radiologically lungs showed prominent bronchovascular markings.

B.S.R. was 10 mm./hour (Westergren). W.B.C. 7400/c.mm., polymorphs 69 per cent, lymphocytes 21 per cent and eosinophils 10 per cent.

Treatment was given on general lines and improvement was observed.

Case 20—D., aged 29 years, male, working in the weaving department for a period of about 16 years came with complaints of cough and dyspnoea for 2 years. He had dyspnoea towards the end of the day's work for which he had to take rest for 10-15 minutes, before he could resume again. The trouble was more during the night shift.

On *examination* he was of poor build but with good nutrition. Chest examination did not reveal and abnormality.

On radiological examination lungs were clear.

W.B.C. 8400/c.mm., polymorphs 70 per cent, lymphocytes 26 per cent and eosinophils 4 per cent.

This was quite an early case ond improved with routine treatment.

Case 21—B.N., aged 35 years, male, working in the carding department came with complaints of cough for 4 years with scanty sputum and dyspnoea while working in the mill on first two days of the week for 1 year. The patient was quite well at home, but had dyspnoea in the mill on two subsequent days following a rest day after a few hours work in the morning.

On examination he was a well built man with poor nutrition. Chest examination showed harsh vesicular breathing only.

Radiologically lung fields were clear.

W.B.C. 7400/c.mm., polymorphs 68 per cent, lymphocytes 30 per cent and eosinophils 2 per cent.

He was kept on general line of treatment and is better now.

Summary

A series of 21 cases has been observed as and when they attended State Insurance Dispensary, Patkapur, Kanpur, during the last 3 years. A

clinical summary of the observations made in this series and investigations relating to the respiratory tract have been noted.

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A NEW ORAL NON-BARBITURATE HYPNOTIC

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Disturbance of sleep is one symptom which frequently troubles the patient very much and a good hypnotic is an asset in the armamentarium of a medical man. When a physical cause for the sleep disturbance is present, eradication of the cause should produce good sleep. When pain is the cause of sleeplessness, analgesic drugs may induce sleep by relieving pain, acting as indirect hypnotics.

Preparations of opium are being used for a long time for producing sleep. Unfortunately opium has got many disadvantages, specially those of addiction and respiratory failure.

Bromides and chloral hydrate are also used as hypnotics but their action is not always very satisfactory.

Barbiturates are the commonest hypnotics used all over the world. They too have drawbacks. A hangover effect is fairly common after their use and the difference between toxic and therapeutic doses is often very small.

Probably paraldehyde is the drug which almost fulfils the standard of an ideal hypnotic. It produces very good sleep for several hours, its toxicity is insignificant, it is excreted fairly in a short time. There is no cumulative effect and addiction is practically unknown. Unfortunately to be surely effective the drug should be given by intramuscular injection which is very painful and may produce severe local inflammation and even abscess formation. Orally it is seldom tolerated. Administered rectally it may produce good effect but absorption from the rectum is uncertain. It also irritates the rectum.

During the last few months, there was an opportunity to try a new nonbarbiturate oral hypnotic in the N. R. Sircar Hospital. Chemically it is alpha-ethyl alpha-phenyl-glutarimide.

The drug was given to 66 patients who had been suffering from sleeplessness. In 6 of them the sleeplessness was due to some definite physical distress, such as severe pain in the chest due to acute dry pleurisy (2 cases), pain in the abdomen due to peptic ulcer, incessant cough due to lung abscess and lung cancer, and severe headache due to tuberculous meningitis (1 case of each). In none of them could the drug produce any significant sleep.

In the remaining 60 cases (40 males, 20 females), there was no definite physical cause for insomnia. The drug was administered after the patients had been in the hospital for some days in order to eliminate sleeplessness due to unfamiliar hospital surroundings which is not an unusual cause of insomnia.

Nearly all varieties of medical conditions were present amongst these sixty patients in which the drug was tried. Altogether, the drug was used 160 times in these patients in the following order —only once in 23 cases, twice in 23 cases, thrice in 10 cases, four times in 8 cases, five times in 4 cases, and nine times in one case. For the sake of comparison, phenobarbitone, potassium bromide, potassium bromide and chloral hydrate and a bland drug, calcium carbonate were also used alternative to alpha-ethyl alpha-phenyl-glutarimide. None of the patients knew what drug they received, but they were told that a drug was being given to produce sleep.

The drug (alpha-ethyl alpha-phenyl-glutarimide) was given in the form of tablets, each containing 250 mg. On 68 occasions, one tablet was found to produce the desired effect, whereas on 92 occasions two tablets were necessary.

On 156 occasions, the drug produced sound sleep ranging from 4 to 9 hours. On 4 occasions (2 cases) it did not have any significant effect. On majority of occasions (144) the drugs produced sleep 15-30 minutes after administration, on 12 occasions it took about 45 minutes.

Side-effects—Side-effects were observed in 6 cases with a dose of 500 mg. Four patients complained of drowsiness and heaviness in the head

next morning for 2 to 3 hours and 2 patients felt sleepy for about 10 hours. On reducing the dose to 250 mg., they had sound sleep without any side-effects next morning.

On all other occasions, the patients had sound sleep and woke up feeling refreshed. No changes in B.P., pulse or respiration rate were observed in the dosage employed. There were no changes in the blood picture or urine, and other routine investigations that were carried out in different cases such as blood urea in nephritis or hypertension, thymol turbity and plasma protein in liver diseases; no deterioration of the original disease was noticed in any case after administration of the drug.

None of the patients showed any tendency to drug addiction and withdrawal of the drug was effected in every case without any symptoms.

On 23 occasions, phenobarbitone (grains 2) was used alternating with the drug in trial. On 4 occasions it did not produce any significant sleep whereas "doriden" did. On 19 occasions phenobarbitone produced 4 to 8 hours' good sleep which usually came 15 to 30 minutes after its administration. 'Hangover' effects with phenobarbitone such as drowsiness and heaviness in the head, headache and sleepiness for next 12 hours were observed.

Potassium bromide (grains 15) was given on eighteen occasions alternating with doriden. It produced fair sleep for 4 to 7 hours on 8 occasions and failed on 10 occasions. Sleep was induced within half an hour after bromide administration. Twice the patients complained of drowsiness and heaviness in the head for 4 hours next morning and only once the patient felt drowsy for the next 10 hours.

Chloral bromide was given alternating with the drug on 14 occasions. On 9 occasions fair sleep was produced for 4 to 6 hours. There was no effect on 5 occasions. Sleep was induced within 30 minutes after administration of the drug. On 2 occasions the patient complained of drowsiness and heaviness in the head for 3 hours after waking up.

Calcium carbonate was given alternating with the drug on 25 occasions. On 4 occasions, fair sleep was obtained for 5 hours, no significant sleep resulted at other times. Induction of sleep occurred ½ hour after the administration of the drug and one patient complained of drowsiness for 2 hours next morning.

Discussion

Doriden has previously been tried by others as a non-barbiturate oral hypnotic. Rushbrooke *et al* (1956) reported that doriden in a dose of 0·5 g. compared favourably with cyclobarbitone 0·2 g. as a hypnotic. Howell (1956) reported a quiet night's sleep of upto 8 hours with a dose 0·5 g.

Morpurgo (1956) reported that with 0·5 g. of doriden, sleep ensued about 30 minutes after administration and generally lasted for 4 to 7 hours. Lane (1955) reported that rapid and effective hypnosis was induced in 43 of 48 patients with a dose of 0·25 to 0·5 g. of doriden and no unpleasant side-effects were noticed. Davis and Gruner (1956) reported that one patient complained of excessive sleepiness the afternoon following his fourth night of doriden (0·5 g. each evening), and in one patient jaundice of unknown cause developed which cleared spontaneously in eight days.

As side-effects a skin rash was noticed by Rushbrooke *et al* (*loc. cit.*) in two patients and by Weston (1956) in three patients. Drug addiction was not noticed by any.

In the present series, 4 to 9 hours of good sleep was observed with a dose of 0·25 to 0·5 g. on 156 occasions out of 160. Sleep was usually induced 15 to 30 minutes after the administration of the drug. Drowsiness and heaviness in the head were the only side-effects noticed in 6 cases with a dose of 0·5 g. and they disappeared when the dose was reduced to 0·25 g.

In comparison with phenobarbitone, this drug seems to have less hangover effects. It can be seen that on 4 occasions, calcium carbonate given as a placebo produced sleep; this must be the effect of suggestion. The number of occasions when doriden produced significant sleep was so frequent that its hypnotic effect could not be regarded as accidental or due to suggestion.

Summary

A new non-barbiturate oral hypnotic, doriden, was tried on 66 patients suffering from various illnesses.

Six patients who had some definite physical cause for the insomnia did not respond.

In 60 patients sleep could be induced in 15 to 20 minutes after administration of the drug and it lasted for 4 to 9 hours.

No side-effect was observed except drowsiness in 6 cases. No evidence of habit formation or withdrawal symptoms were noticed.

A comparison has been made in some cases with phenobarbitone, potassium bromide, chloral hydrate and potassium bromide and a placebo (calcium carbonate).

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CASE NOTES

NEURILEMMOMA OF THE APPENDIX

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A perusal of the available literature has failed to disclose another distinct instance of a neurilemmoma of the appendix after the one reported by Peritz in 1930 and accepted by Stout (1935) in his review.

The following case of appendicular neurilemmoma is therefore considered worthy of report.

CASE REPORT

A forty-five year old female was admitted to the Chittaranjan Cancer Hospital, Calcutta, for gradual loss of appetite and flatulent dyspepsia for about one year. For about the same time, she complained of occasional attacks of pain in the right hypochondrium and the epigastrium. The pain was dull aching in character and had no relation to food. The pain radiated occasionally to the back and sometimes to the left shoulder. The pain used to persist for several hours and relief could not be ascribed to any specific drug or measure. For the last six months, the pain recurred with increased frequency (4 to 5 times a month). There was no vomiting and the patient was constipated throughout the whole episode. There was no history of haematemesis or melaena. She had suffered from jaundice 23 years previous to this illness and *Esch. coli* infection of the urinary tract (post-partum) about 14 years ago. She is a chronic sufferer from bronchial asthma for the last 10 years. Her weight had been steadily decreasing.

The family history was not significant.

On examination she appeared a slightly obese female of average build. The skin was of normal colour with no subcutaneous nodule. A few pigmented moles and haemangiomata were scattered over the body. The abdominal panniculus adiposus was prominent and the musculature was lax. On deep palpation some vague tenderness was elicited in the right hypochondrium and the epigastrium. There was no rigidity and no lump was palpable anywhere in the abdomen. There were coarse rales at the bases of both the lungs. Rectal and pelvic examinations revealed no abnormality. No supraclavicular or cervical lymph node enlargement was detected.

Laboratory investigations—Stool, urine and blood along with serology failed to reveal any abnormality. Fractional test-meal with 7·5 per cent alcohol and insulin-histamine test revealed an extreme degree of hypochlorhydria. Cytological examination of the centrifugalised gastric wash failed to show any malignant cell after staining the smear according to Papanicolau's method.

X-ray examinations—Barium meal investigation of the gastro-intestinal tract revealed no abnormality. Cholecystography disclosed some delay in the emptying of the gall-bladder. Skiagram of the chest showed enlargement of the right tracheobronchial lymphnodes.

Exploratory laparotomy—The stomach, duodenum and colon were normal. The outer surface of the gall-bladder was opaque and had a yellowish tinge. Three abnormal peritoneal bands were found anchoring the neck of the gall-bladder to the duodenum and the transverse colon. The appendix was very long and tortuous with a bulbous end. The peritoneal bands anchoring the neck of the gall-bladder were cut between ligatures and cholecystectomy with appendicectomy was done as usual. What appeared to be the bulbous end of the appendix, on closer examination, was found in reality to be a yellowish white oval fleshy swelling situated just below the tip.

The post-operative recovery of the patient was uneventful except for a moderately severe attack of bronchial asthma from the sixth to the eighth post-operative day. The patient has

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been followed up for the last two years and so far is free from any abdominal complaint.

Pathological examination—Gross examination revealed a fleshy, oval, encapsulated tumour with the longest diameter measuring about 1·5 cm. The cut surface presented a whorled appearance. There was no area of softening and haemorrhage. For histological examination, pieces were taken both from the periphery and centre of the tumour and in addition to the routine eosin and haematoxylin staining, sections were stained by van Gieson's picro-acid fuchsin method and Gomeri's silver method for reticulum.

Histological examination showed the tumour to be demarcated by a connective tissue capsule with projections into the interior. The tumour proper was composed of spindle-shaped cells with oval nuclei showing a distinctive palisade pattern (Fig. 1, *vide* Plate). There was a profusion of collagen and reticulin fibres which tended to form interlacing bundles. No mitosis was seen. The picture presented was consistent with that of a neurilemmoma of Antoni 'Type A'.

Discussion

The discovery of the tumour in this case was quite accidental. The abdominal symptoms were vague and none pointed to the appendix in particular. There was a concomitant lesion of the gall-bladder to which some of the symptoms, at least, may be attributed.

The neurilemmoma in this patient was the only neurogenic tumour, there being no other tumour of this origin either on her person or in the family.

By its location and gross appearance the tumour looked like a carcinoid. On histological examination, the parallel groups of spindle cells with palisading of their nuclei along with the interlacing bundles of collagen and reticulin fibres presented on unmistakable appearance characteristic of neurilemmoma. Absence of myofibrils after appropriate staining procedures excluded the possibility of leiomyoma with which neurilemmoma may be confused (Golden and Stout, 1941).

As was originally pointed out by Stout (1935) this tumour has a marked selectivity of distribution over the body, none or only a few cases having been reported in the site of urogenital organs, lungs, oesophagus, appendix, rectum etc. What this selectivity is due to, is still unknown.

In the type, which is called ganglioneuroma there is a hypertrophy of the whole neuromuscular complex, leading to the formation of what is better known as giant appendix. The lesions associated with 'neuroappendicopathy' are also clearly separable from this case of a distinctly encapsulated neurilemmal tumour reported here.

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KARTAGENER'S SYNDROME

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This case is presented as there are only a few cases of Kartagener's syndrome reported in the Indian literature, and because this is possibly the first such case to undergo lobectomy in India.

Case Report

R. P., male, aged 30, was admitted to hospital on 5-11-1955 with a history of cough of 8 years' duration. This cough was dry at first but later it was accompanied by expectoration. At the time of admission he was bringing up 2 to 3 oz. of mucopurulent sputum which was foul-smelling. He had occasionally noticed wheezing in the chest for the past 3 years.

On examination there was slight clubbing of the finger nails. On auscultation of the lungs medium crepitations were heard at the left base. The apex beat was felt on the right side in the fifth intercostal space on the right midclavicular line, and a normal area of cardiac dullness was made out on percussion of the right side of the chest. Heart sounds were normal in all the areas. The B.P. was 110/70 mm. of Hg. The liver dullness was appreciated on the left side by percussion of the left lower part of the chest. Traube's space was made out on the right side.

Investigations—Skiagram of the chest revealed dextrocardia. There were increased markings in the left hilus especially towards the left base (Fig. 1, *vide* Plate).

Skiagram of the nasal accessory sinuses showed frontal sinuses to be small, and the maxillary sinuses showed evidence of thickening of the mucous membranes, with fluid levels (Fig. 2, *vide* Plate).

A barium meal examination showed the stomach to be on the right side.

A bronchogram showed the branches of the left bronchus to be crowded together with tubular and cystic dilatation (Fig. 3, *vide* Plate).

E.C.G. showed complete reversal of all complexes in Lead I and interchange of Leads II and III.

Treatment—The patient was given injections of procaine penicillin 6 lakhs twice a day for 10 days prior to operation. A left thoracotomy was done by Dr. R. H. Betts on 29-11-1955. It was found that the lung in the left hemithorax consisted of three lobes. The middle and lower lobes were found to be bronchiectatic, and were removed. The patient continued to have penicillin postoperatively and was also given injections of streptomycin 1 g. once a day. The postoperative period was uneventful. The patient was discharged on the 16th postoperative day with cough and expectoration considerably diminished.

Pathological examination of the removed lung—Macroscopic: The specimen was anatomical right middle and right lower lobes which were hard and fibrotic. On section there was marked dilatation of the bronchi of both lobes (Fig. 4, *vide* Plate), the middle being small and atelectatic. There were also a few cystic areas, especially near the diaphragmatic surface.

Microscopic: The lung showed marked dilatation of the bronchi with dense inflammatory exudate in the walls of the bronchi. Some of the cystic areas showed well marked squamous metaplasia in the wall. The main bronchus showed inflammatory cells in the submucosa.

Follow up—The patient was seen 1½ years after discharge from the hospital. He had no cough and the lung revealed no adventitious sound.

Discussion

The association of situs inversus, sinusitis and bronchiectasis is now generally referred to as Kartagener's syndrome or triad. However, it was Siewart (1904), quoted by Adams and Churchill (1937), who first published a report of a case with this pathological constellation. His report was in German and the seven reports of this syndrome following it were also in that language (Adams and Churchill, 1937). Although two of these reports precede Kartagener's (1933) chronologically, "to this author was left the merit of the interpretation and aetiological correlation of the different components of this system that had undoubtedly escaped the attention of those who believed they were describing a mere morbid casual association" (Taina *et al*, 1955). It was only in 1937, that the first report of this syndrome appeared in the English language (Adams and Churchill, 1937). As regards the Indian literature I have come across three case reports of Kartagener's triad. They are by Chatterjee (1951), Baruah and Chari (1952), and Raman *et al* (1955). In the case reported by Baruah and Chari (*loc. cit.*) besides the triad there was an associated bronchogenic carcinoma. Taiana *et al* (1955) after a review of the world literature found 104 cases reported upto 1955. However, they have somehow missed the three cases in the Indian literature cited above.

This interesting syndrome brings up the controversial issue of the aetiology of bronchiectasis and seems to shed some light on it. Many authors now believe that bronchiectasis is acquired following a pulmonary infection. Suerbruch, however, championed the congenital theory and contended that 80 per cent of the cases of bronchiectasis had such an origin. Kartagener (1933) maintained that bronchiectasis in combination with situs inversus lends support to Suerbruch's view. Kartagener and Horlacher (1935), quoted by Adams and Churchill (1937), found 6 cases of bronchiectasis in 30 cases of situs inversus, an incidence of 20 per cent, and Torgersen (1947) found 10 cases of bronchiectasis among 129 cases of situs inversus, an incidence of 8 per cent. Adams and Churchill (1937) found 23 cases diagnosed as situs inversus during a period of 52 years (1886 to 1937). Five of these had bronchiectasis an incidence of 21·7 per cent. During the same period the incidence of bronchiectasis in the general hospital population was 0·3 per cent. Therefore the incidence of bronchiectasis was 72 times more common in patients with situs inversus than in the general hospital patients. Olsen (1943) during a period of 22 years (1920-41) found a total of 85 patients who had situs inversus at the Mayo Clinic. Definite evidence of bronchiectasis was present in 14 of these, an incidence of 16·5 per cent. During the same 22 year period under consideration a diagnosis of bronchiectasis was made in less than 0·5 per cent of the total number of patients who registered at the Mayo Clinic. Thus the incidence of bronchiectasis was 33 times more common in patients with situs inversus than in the general run of patients seen at the clinic. These figures show that the association of bronchiectasis in patients with situs inversus is not a chance occurrence and that since the latter condition is a congenital anomaly it is reasonable to conclude that the bronchiectasis has a similar origin. Most authors reporting isolated cases of this syndrome say that the bronchiectasis in Kartagener's triad is due to a congenital weakening of the bronchial wall which is brought out clinically by an acquired infection. This theory has been proposed by some for the pathogenesis of all cases of bronchiectasis and according to Gunn (1953) will be very difficult to disprove.

With regard to the occurrence of sinusitis as a component of Kartagener syndrome Adams and Churchill (1937) say "As over 90 per cent of all cases of bronchiectasis have symptoms or signs of infection of the accessory nasal sinuses little emphasis can be placed on the co-incidence of these two components of Kartagener's triad. Although the hypothesis that sinusitis precedes and causes bronchiectasis has been a popular one we have personally been unable to subscribe to this view except in occasional instances. It is just as rational to consider the bronchiectasis primary and the sinusitis secondary or both conditions due to a common underlying element". Richards (1944) has pointed out that underdevelopment of the nasal accessory sinuses may be a feature of this syndrome. The patient reported above had underdevelopment of the frontal sinuses as well as maxillary sinusitis.

Mass radiography in the control of tuberculosis is bound to uncover many more cases of dextrocardia. Some of these may be cases of Kartagener's syndrome.

The treatment of Kartagener's syndrome is to remove the affected lobes surgically after a course of antibiotics. In our patient the middle and lower lobes were resected. He was symptomless and in excellent general health one and half years after the resection.

ACKNOWLEDGMENT

I am grateful to Dr. R. H. Betts for permitting me to report this case.

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ILEOCYSTOPLASTY IN A CASE OF CONTRACTED URINARY BLADDER FOLLOWING TUBERCULOSIS

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Contracted urinary bladder is a miserable condition because of frequency of micturition. Various operations have been devised to enlarge the capacity of the bladder in this condition. Pyrah and Raper (1955) described the use of a closed loop of ileum for ileocystoplasty in patients who had contracted urinary bladder due to interstitial cystitis or tuberculosis. We recently had a case of contracted urinary bladder following tuberculosis where ileocystoplasty was done. The case is reported.

CASE REPORT

A, aged 30, was admitted on 1-10-56 with the complaints of frequency of micturition and associated burning sensation for the last 4 years. The patient had to run to void urine every 15-20 minutes. History of occasional haematuria present.

On examination the patient was afebrile. There was no sign of tuberculosis.

Laboratory investigation—Urine contained albumen, pus cells and R.B.C. and was acid in reaction. E.S.R. was 20 mm./1 hour. Blood urea was within normal limits. Urine culture could not be done for want of facilities.

The *skiagram* and *pyelogram* showed no abnormality in the urinary tract except for the bladder which appeared to be contracted. Less than 1½ oz. of water could be put into the bladder and a satisfactory cystoscopy was not possible.

The patient had a full course of streptomycin and INH but had no relief beyond improvement in the microscopical appearance of the urine and disappearance of strangury.

Operation—The patient was put up for operation and a loop from the terminal part of the ileum about 4″ long was isolated with its blood supply intact. The continuity of the gastro-intestinal tract was restored by an end-to-end anastomosis of the proximal and distal ends of the ileum. The isolated loop of the ileum was closed at the two ends and thus a 4″ long closed tube with its blood supply intact was obtained.

A 1½″ long longitudinal cut was made along the antimesenteric border in this tube. Similarly the bladder was also cut open through an incision and an anastomosis in two layers was done, the first layer being through and through and second being seromuscular. An indwelling catheter was left per urethra.

During the post-operative period urine was draining through the indwelling catheter which was removed after 14 days. The frequency of micturition was the same as before removal. The patient was encouraged to take less of fluids and to retain the urine as long as possible. In two weeks' time the patient was able to retain urine for 3-4 hours and the amount passed each time was 7-8 ounces. A cystogram was taken at this stage to show the bladder and the anastomosed ileum.

COMMENTS

The technique of ileocystoplasty employed in this case is very simple. The result has also been encouraging. When the operation is done on a contracted bladder following tuberculosis, the disease must be quiescent. The operation is not advisable when there is evidence of active tuberculosis in the upper urinary tract.

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JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION
CALCUTTA, OCTOBER 16, 1957

CALCUTTA SCHOOL OF TROPICAL MEDICINE :

A Decade in Retrospect

The Calcutta School of Tropical Medicine was established in 1921 and was supported liberally by the Government, private enterprises and certain Zamindari estates, during the first 15 years of its existence. It soon won All-India and even international reputation as a centre of post-graduate teaching and research on tropical diseases and parasitology. But for several years before 1947, the School was allowed to be progressively depleted of its experienced and promising staff and vacancies were not filled up unless it suited the reactionary policies of the then Government of Bengal. The financial support of the Government was inadequate and the resources of the School, particularly of its Endowment Fund, were depleted gradually, more so during the years of the Second World War. In 1947, the institution was actually passing through a near crisis. There was serious depletion of personnel ; most of the senior posts were filled up by stop-gap arrangement ; the posts of assistant professors were kept vacant and the financial position was very unsatisfactory. The only redeeming feature in this depressing picture was the fact that a small band of workers continued their researches under trying conditions and their contribution to science maintained the tradition of the institution.

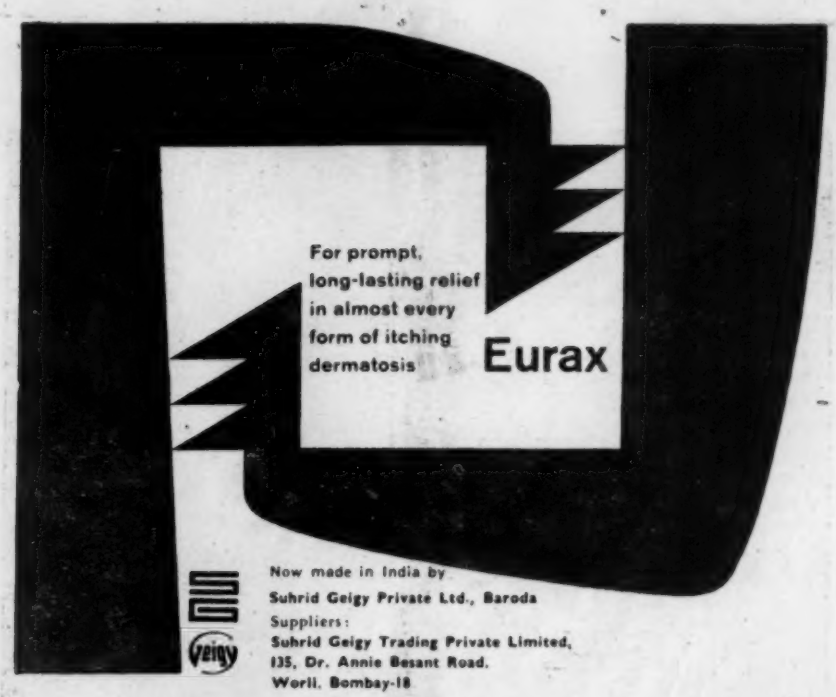
In 1949, the management of the school was vested on a Governing Body of officials and non-officials and during the following years there was a progressive improvement in State aid to the institution. Modern equipment was gradually provided, vacant posts were filled up ; as many as ten posts for teaching and research work besides those of assistants in the laboratories, the hospital and the office were created and some of the existing posts were upgraded. New laboratories, viz., the virus research laboratory, and the insectarium were opened, thus providing for increased facilities for research. As many as 12 members of the staff were admitted to the M.D. or D.Phil of the Calcutta University. A total of 31 research fellowships and scholarships were granted by different organisations or individuals during the period under review.

This progressive policy of the State Government has yielded valuable returns. The activities of the School have increased considerably. The large volume of researches on tropical medicine and basic sciences that has been emanating from the institution has rendered the publication of a quarterly *Bulletin* essential in order to record these briefly. The monthly Clinical Meetings of the School are well attended by the members of the profession and the various other meetings of the staff provide for coordination in the carrying out and assessment of research activities. There has been some upgrading of post-graduate teaching with the introduction of nine months' course for the D.T.M. & H. under the Calcutta University and a new course of study for the Diploma in Clinical Pathology has been introduced in order to provide fully trained clinical pathologists for the country. There has been considerable improvement in providing medical relief to the people by organising new out-patients' clinics, some working in the afternoon dealing with specified conditions, and opening of new wards in the hospital for tropical diseases.

The researches carried out during the decade have been briefly described by the heads of the different departments in a special issue of the *Bulletin*. These reviews will be read with benefit by those interested in different branches of medical sciences. It is apparent that a considerable volume of research work has been carried out on the different aspects of various tropical diseases prevalent in this country, viz., malaria, tropical splenomegaly, kala-azar, epidemic dropsy, tropical eosinophilia, amoebiasis, chronic bowel diseases, cholera, enteric fevers, naga sore, blood diseases, nutritional diseases, filariasis, virus diseases, various skin diseases, leprosy, etc. Researches of fundamental nature were carried out on various parasitic protozoa, helminths, some fungi, the leprosy bacillus and certain insects of medical importance. The cytochemical pattern and the significance of different chemical groups in the life processes of parasites, changes induced by drugs, etc. were worked out. Valuable contributions were made in the investigation of indigenous drugs and working out the pharmacology of certain indigenous drugs and synthetic compounds.

Some of the contributions made by the workers of the School during the decade that are of general interest to the profession are briefly referred to.

Extensive investigations on the chemotherapy of malaria enabled the proper dosage schedules to be worked out for the treatment of acute attacks and of prevention of malaria in the semi-immune rural population in the country. It was concluded that under the present circumstances, for the treatment of acute malaria where efficacy and local availability are important considerations, quinine should be employed. Natural resistance of *P. falci-*



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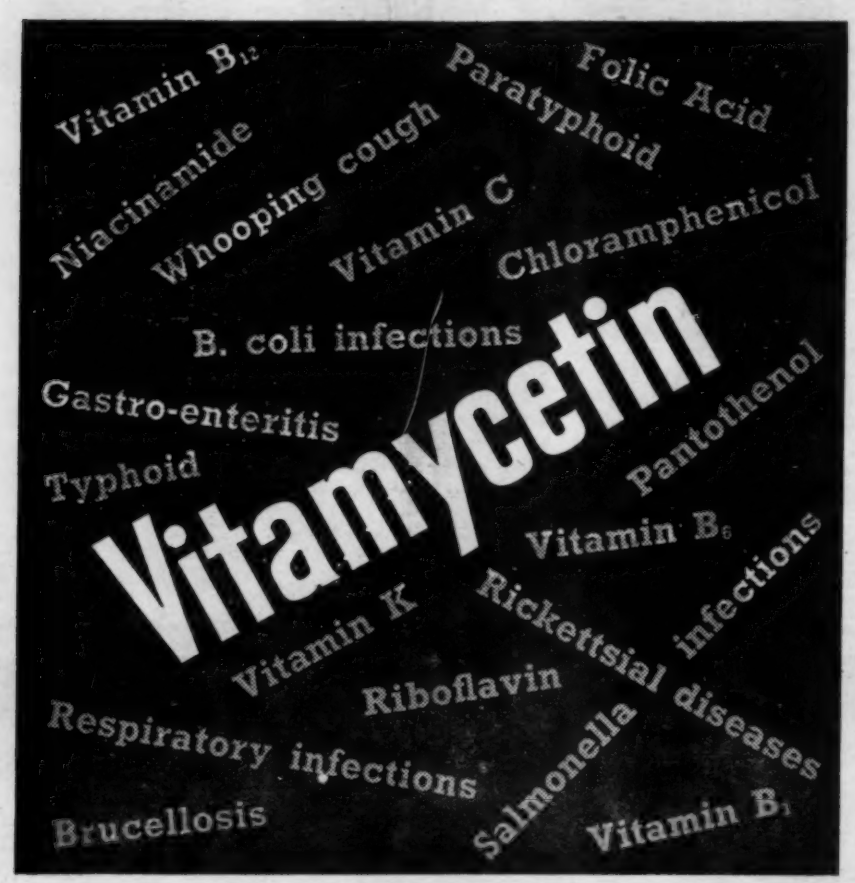

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parum to paludrine was described for the first time and it was shown that administration of this drug to a patient with falciparum malaria did not prevent development of the parasite in the mosquito fed on the patient and transmission of infection by the bite of these mosquitoes to a human volunteer. Bengal splenomegaly or tropical splenomegaly that constituted a menace to rural health was investigated and its aetiology, treatment and prevention worked out by experimental, clinicopathological and epidemiological study. The condition started as chronic malaria and later hypersplenism developed leading to anaemia, leucopenia and thrombocytopenia, still later hepatic changes supervened and led to portal obstruction and complications. It is of interest that the condition is on rapid decline as a result of antimalarial measures, thus supporting the aetiological basis of malaria in this condition.

Epidemic dropsy was produced in experimental animals and a method of assessing therapeutic agents developed. It was found that hydrocortisone gave encouraging result in prevention of experimental epidemic dropsy.

Tropical eosinophilia was investigated in detail and it was concluded that the condition was of the nature of infection-allergy, the infection being probably of a parasitic nature. Diethyl carbamazine has been found to be effective and corticosteroids to cause immediate but temporary relief. The former has been recommended in treatment in preference to arsenical injections.

The aetiopathology and treatment of nutritional macrocytic anaemia, dimorphic anaemia and anaemia in pregnancy were worked out. Haemoglobinopathic anaemias were shown to be fairly common in this country. The presence of haemoglobin E and occasionally haemoglobin S in thalassaemic individuals was described and the pattern of genetic inheritance of these abnormalities were worked out.

Hydroxystilbamidine, a new aromatic diamidine compound, was introduced in the treatment of kala-azar and it proved to have a powerful curative action. Drug resistance in kala-azar was found to be due to excessive hypersplenism that responded only to splenectomy preceded and followed by chemotherapy. The necessity of prolonged specific treatment even after splenectomy indicated that the parasite itself was probably relatively drug resistant. A good deal of work has been done on post-kala-azar dermal leishmaniasis, a condition where parasites grow and multiply in the skin giving rise to a variety of skin changes.

A proved case of generalised histoplasmosis in an Indian was reported for the first time from the School in 1953. Another case was admitted and a third diagnosed in 1957, indicating that histoplasmosis in its dangerous generalised form was not unknown in this country.

A considerable amount of pioneer investigations on the treatment of leprosy with the new chemotherapeutic drugs was carried out in the institution and the course of treatment suitable for different types of leprosy seen in this country was worked out. It was shown by using isotope-tagged (with S_{35}) diaminodiphenyl sulphone, that it was localised selectively in leprous tissue. A new antigen was prepared from Kedrowsky's acid-fast bacillus for intradermal test in leprosy; it gave results identical with refined lepromin prepared from infected human tissues.

Significant and important contributions were made on the pharmacology of rauwolfia alkaloids which were shown to possess renal vasodilator action and a sedative action on the hypothalmus at a site different from that of certain tranquillising drugs and sedatives. The site of action of chlorpromazine was worked out by means of extensive neuropharmacological investigations to be in the hypothalamus, rostral to the site controlling diuresis, stress lymphopenia etc.

Investigations on a large number of indigenous drugs showed that many of the medicinal plants included in the Indian Pharmacopoeia could be grown in this country. Ipecac, cultivated at Rongo (Darjeeling district in West Bengal) contained larger or comparable amounts of active principles than many imported plants. Diosgenin, a drug intermediate suitable for the preparation of certain steroid hormones including cortisone, could be obtained in high yield from a number of jungle yams growing in India. Progesterone has been prepared from diosgenin thus isolated.

Some of the other interesting researches were on the value of anti-human serum floccule in the treatment of certain allergic diseases, those on animal skin diseases communicable to man and treatment of cutaneous tuberculosis, cultivation of the fusiformis of naga sore in the hen's eggs and the treatment of naga sore with streptomycin.

The School has during the last 37 years trained a large number of medical personnel who with their specialised training have spread out throughout the country thus helping materially to raise the status of practice of tropical medicine in India[1].

We express our appreciation of the contributions made by the workers of the institution and expect that with the continuation of the present State policy of upgrading existing research institutions steady all-round progress will continue.

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CURRENT MEDICAL LITERATURE

Serum Glutamic Oxaloacetic Transaminase Activity

NYDICK AND OTHERS (*Circulation*, **15**: 324, 1957) in dealing with variations in serum glutamic oxaloacetic transaminase activity in experimental and clinical coronary insufficiency, pericarditis and pulmonary infarction observe:

The serum activity of the enzyme, glutamic-oxaloacetic transaminase, was not increased following experimental myocardial ischaemia in dogs unless myocardial necrosis was found at autopsy. The SGO-T activity remained within normal limits in 35 of 50 patients with status anginosus or severe coronary insufficiency accompanied by ST segment and T-wave abnormalities. The SGO-T activity appears to be useful in establishing the presence or absence of myocardial necrosis in patients with severe recurrent substernal pain.

The SGO-T activity was within normal limits in experimental pericarditis unless subepicardial necrosis was found at autopsy and the SGO-T activity remained within normal limits in 9 of 11 patients with acute pericarditis of various aetiologies. In 2 patients brief and insignificant elevations (maximum 56 units) occurred.

In 6 of 7 patients with pulmonary infarction no alterations in transaminase levels were found. An insignificant rise was seen in the seventh patient.

The SGO-T activity appears to be useful in determining the presence or absence of acute myocardial damage following acute myocardial infarction, coronary insufficiency and pericarditis. It can be a valuable aid in the differential diagnosis of chest pain.

Distribution of Pain in Myocardial Infarction

KREINES (*Circulation*, **15**: 348, 1957) from analysis of the clinical records, electrocardiograms, and autopsy protocols of 104 cases of myocardial infarction were carefully examined to determine if there is an association between the location and extent of involved myocardium and the radiation of pain to "atypical" sites such as the back and epigastrium. No association was found between location of myocardial infarction in the posterior or diaphragmatic wall of the heart and radiation of pain to the back and abdomen. A statistically significant association was found between the occurrence of massive myocardial infarctions and radiation of pain to the back and epigastrium. It is suggested that the size of a myocardial infarction may be one of the factors determining the radiation of pain.

Cardiovascular Disturbances in Chronic Severe Anaemia

SANGHVI AND OTHERS (*Circulation*, **15**: 373, 1957) from a study of cardiovascular disturbances in 60 cases of chronic severe anaemia seen in S.M.S. Medical College Hospitals, Jaipur, observe:

Two patterns of these disturbances were seen although a clear line of demarcation between the two could not be drawn. In one tachycardia, increased velocity of the blood flow, little pulmonary congestion, and increased cardiac output were noted, particularly in the presence of congestive failure. In the other, there was either a normal or a slow cardiac rate, comparatively diminished velocity of the blood flow, more pulmonary congestion, and either a normal or a diminished cardiac output, even in the presence of failure. The incidence of congestive failure was high. No cause could be discovered for the two patterns of disturbances or for the high incidence of congestive failure.

Effect of Morphine and n-Allyl Normorphine

MOYER AND OTHERS (*Circulation*, **15**: 379, 1957) gives in the following lines the summary of their observations on the effect of morphine and n-allylnormorphine on cerebral haemodynamics and oxygen metabolism:

The effect of 60 mg. of intravenously administered morphine has been studied in human volunteers. Although variations occur in individual patients, cerebral blood flow for the group is not altered significantly following the administration of morphine, but cerebral oxygen uptake ($CMRO_2$) is depressed to a significant degree in all. The reduction in $CMRO_2$ is associated with a reduction in arterial oxygen content, as well as a reduction in the extraction of oxygen from the blood circulating through the brain. These effects are rapidly (but only partly) reversed following the administration of n-allylnormorphine.

Arterial blood oxygen saturation and oxygen content are decreased, while content and partial pressure of carbon dioxide are increased following the administration of morphine. The alterations in the blood flowing to the brain would tend to increase cerebral blood flow. This response was observed in a few instances, but was inconstant. The alterations in blood oxygen and carbon dioxide concentrations resulting from the central respiratory depressant effects of morphine are reversed with n-allylnormorphine.

Sodium Chloride Intake in Hypertension

DAHL AND LOVE (*J.A.M.A.*, **164**: 397, 1957) from the analysis of their study on the aetiological role of sodium chloride intake in essential hypertension in human observe:

Among 1,346 adults who were classified according to their sodium chloride intake at the table, there were only 135 classed as having a low intake, while there were 630 and 581 in the average-intake and high-intake groups respectively. The 105 persons with hypertension were distributed among the salt-intake groups in nonrandom fashion as follows: low intake, 1; average intake, 43; and high intake, 61. Tested by the chi-square method, the probability of such a distribution of hypertension occurring by chance was found to be less than 1 in 1,000. The group with low salt intake had significantly less and the group with high salt intake significantly more hypertension than would be expected from random distribution.

By dividing all individuals into overweight and nonoverweight groups in addition to the sodium chloride categories, the following statistically significant ($p<0.01$)

conclusions can be derived: 1. Individuals who are not overweight but who are on a high-salt diet will have several times the incidence of hypertension found in similar individuals on a low-salt diet. 2. Among individuals who are on a high-salt diet, those who are overweight will have significantly more hypertension than will those who are not overweight. 3. Those individuals who are both overweight and on a high-salt diet will have a much greater incidence of hypertension than will individuals not overweight and on a low-sodium diet. The hypothesis is submitted that the level of sodium intake is the primary aetiological factor in the development of essential hypertension.

Hypertonia or Uneventful High Blood Pressure

EVAN (*Lancet*, **2**: 53, 1957) gives in the following lines the summary of an address given during the Harveian Tercentenary meeting held in London:

The blood pressure was first examined in 400 healthy male recruits entering military service, and a record of blood pressure was made some ten years subsequently in four other groups of cases. The first group consisted of 50 young men in whom the blood pressure was normal. The second held 50 young men in whom the blood pressure was somewhat raised so that the systolic was 180 mm. Hg or over and/or the diastolic was 100 or over. The third group was made up of 50 older subjects of both sexes who showed higher blood pressure values so that the systolic pressure was 200 mm. Hg or over and/or the diastolic pressure 110 or over, but where cardio-arterial changes were absent. The fourth group included 50 older patients of both sexes with blood pressure readings of the same order as patients in the third group, but in whom cardio-arterial changes were present. The last two groups were assembled during the same period and were consecutive cases presenting for routine examination. The assembling of the 50 cases of hypertonia was completed two months ahead of the hypertension group, establishing the commoner incidence of hypertonia.

A study of these five groups emphasised the need to revise the views customarily held on the reading which may be accepted as a natural blood pressure value in healthy subjects. It became clear that moderately high values in young people did not presage a significant hypertension in later life, and that the high blood pressure met with in older adults carried no sinister meaning provided it was of the mutable kind and not associated with cardio-arterial derangement, instanced specially by refractory contraction of the lesser arteries and electrocardiographic proof of left ventricular hypertrophy.

In order to distinguish this innocent condition from arterial hypertension where an abiding high blood pressure is associated with specific cardio-arterial changes, it is apposite to apply to it a distinctive name, and hypertonia is here proposed for it.

There are many reasons why a recognition of hypertonia as a separate clinical entity is needed. Chief among them is the favourable prognosis associated with hypertonia and which is in sharp contrast with the serious outlook in patients with arterial hypertension. This differentiation will avoid unwarranted invalidism, which is now rife and the inevitable outcome of an erroneous diagnosis, and it will particularly avoid the unjust loading of premiums for life assurance which is such common current practice.

To misjudge in diagnosis is to err in treatment. To mistake hypertonia for hypertension may not cause a life to burn out, but it will make it burn low; the addition of heroic hypotensive measures when unneeded is certain to subdue the flame. It does not cause surprise that therapy of any sort will appear to ameliorate symptoms that may arise in association with hypertonia in that they are incidental to it. If a condition is innocent enough, as this is, not to maim through the years, we should guard against accrediting a symptomless period to any potion fortuitously prescribed at the time. Moreover, it is imprudent to dispense medicine continuously to a patient which serves as a constant reminder of a disability which is more imaginary than real. Even in the case of true arterial hypertension, reflection on the underlying pathology in the form of severe closure of so many essential arteries by intimal proliferation, prevents any surprise that neither product of test-tube or crucible halts, nor delays materially, the unfavourable course of the disease.

A contribution to the improved management of patients described here is to oppose a diagnosis of arterial hypertension in any where the blood pressure is raised, even to substantial levels, but where it proves to be mutable, and where a normal electrocardiogram endorses the absence of left ventricular hypertrophy.

Hyperaldosteronism in Heart Disease

WOLFF AND OTHERS (*Lancet*, **2**: 63, 1957) from the study of the excretion of aldosterone and of sodium in 40 patients with various forms of heart-failure before, during, and after treatment with digitalis, diuretics, and sodium restriction of various degrees observe:

Two-thirds of the untreated patients with generalised cardiac hydrops showed increased aldosterone activity and considerable retention of sodium. The remaining third showed normal excretion of aldosterone and were in or near sodium equilibrium at the time of study.

In patients with "left-sided failure" the excretion of aldosterone and of sodium was usually normal, whereas most patients with "right-sided failure" showed increased aldosterone activity and considerable sodium retention.

Different responses of aldosterone activity to treatment of heart and oedema were observed, and their probable causes are discussed.

Hyperaldosteronism in heart-failure is primarily evoked by changes in cardiovascular haemodynamics. The failure to decrease aldosterone activity after the retention of sodium and water mainly contributes to the ever increasing accumulation of oedema in hydropic heart-disease.

Increased aldosterone activity and sodium retention were observed in the first week following myocardial infarction. This response of the sodium-conserving mechanism apparently tends to restore the circulating volume reduced by hypovolaemic shock (*Authors' summary*).

Chemotherapy in Tuberculosis of the Hip

STEVENSON AND OTHERS (*Tubercle*, **38** : 164, 1957) in emphasising the value of chemotherapy in the treatment of tuberculosis of the hip in children observes :

Of 18 children with intra-articular disease, treated for the first time conservatively with chemotherapy, nine retained a full range of movement, one almost full, one 100° flexion, and one 30° flexion. Only six proceeded to fibrous ankylosis. This compares most favourably with a series of 39 such children treated before the advent of chemotherapy, of whom only three retained a small degree of flexion, the rest proceeding to fibrous ankylosis or operative arthrodesis. The failures in these cases of intra-articular disease treated with chemotherapy superimposed upon routine conservative treatment are attributed to delay in the starting of chemotherapy, too short conservative treatment, failure to drain associated extra-articular disease, and traumatic reactivation. The duration of conservative treatment in these cases was five to twenty-three months, with an average of just over twelve months. This is half the average time for such cases before chemotherapy became available. Of six patients with extra-articular disease, four retained full movement, one 120° flexion and one 90° flexion. The average length of conservative treatment in these cases was seven months—one-third of that required in the pre-chemotherapy era. It is pointed out that many of the children in the early days received only one drug for three months—now recognised to be inadequate therapy. All patients are now given at least six months' triple drug treatment, and occasionally nine months.

Diabetes Mellitus and Anaesthesia

In the preparation of diabetic patients for general anaesthesia, glucose is often given by mouth. It is of the greatest importance to prevent both hypoglycaemia and ketosis in these patients, but it is equally imperative not to overlook the potential dangers of regurgitation and vomiting when glucose is given shortly before anaesthesia is induced. During the past few years, these events have achieved some notoriety as causes of death and other complications in all patients given a general anaesthetic, including some with diabetes mellitus.

The normal emptying time of the stomach after a solid meal is about four hours, and up to two hours after fluid. Thus preoperative oral carbohydrate, if it is to serve any useful purpose, must be given so close to the time of anaesthesia that it becomes a potential hazard, unless the stomach empties quickly. In fact, it may well empty slowly because of fear, premedication, and the glucose itself.

King (*Anaesthesia*, **12** : 30, 1957) has lately confirmed that the hazard is a real one. 200 ml. of water, containing phenol red and 50 g. glucose, was given to each of a group of fasting healthy young adults, and the stomach was completely aspirated at intervals varying from fifteen minutes to two hours. It was found that, on the average, the meal was diluted to about twice its volume, but that after two hours only 46 ml. of fluid, containing 0·3 g. glucose, remained. A similar solution, but containing no phenol red, was given to each of 20 diabetic and non-diabetic patients two hours before operation, the stomach was aspirated two hours later. Previous investigations had shown that gastric function was normal in all these patients, yet in 10 of them volumes ranging from 100 to 265 ml. (average 146 ml.), containing 2·10·2 g. glucose was removed from the stomach. Thus, there seems little doubt that preoperative glucose solutions given by mouth are potentially dangerous and unlikely to prevent hypoglycaemia.

The answer is to give the glucose intravenously or not at all. A single intravenous injection of glucose given not more than an hour before the induction of anaesthesia may be enough for a minor operation on some diabetic patients; but in most cases King recommends continuous intravenous glucose over a number of hours, including the postoperative period, when there may be nausea and vomiting. Soluble insulin should be given in divided doses every four or six hours. King believes that this method is the safest and most effective means of ensuring good control for all diabetic patients undergoing emergency or major operations, and for patients with severe diabetes whatever the operation. Many mild diabetics need no glucose preparation for a small operation, provided it is carried out early in the morning and an adequate intake of carbohydrate is ensured after operation.

King has clarified a subject which is often an irritation to anaesthetists, but he adds a wise reminder that dogma has no place in the control of diabetic patients treated by surgery : each case must be considered individually.—Annotations, *Lancet*, **1** : 463, 1957.

CURRENT TOPIC

TETANUS—A PRESENT-DAY ANALYSIS

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PART ONE

The universal presence of the causative organism of tetanus, namely *Clostridium tetani*, throughout the inhabited world no doubt has plagued mankind since his beginning. This organism is a natural inhabitant of the intestinal tract of man and animals and, consequently, perpetually reseeds man's environmental soils. Thus, contamination of his frequent wounds, large or small, leaves man a vulnerable candidate for tetanus. It is surprising, yet fortunate, that this disease does not occur in larger numbers of the world's population.

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The scope of this paper does not allow detailed presentation of the many facets of the problem, although an attempt will be made to include information that appears pertinent. An extensive list of references is not appended because a number of recent articles have contained large bibliographies concerning various phases of tetanus. Because tetanus and its management are controversial subjects, it is anticipated that differences of opinion will arise among those who read this paper; however, it is hoped that with disagreement will come greater enthusiasm and an effort to clarify some of the muddled issues characteristic of this disease.

Historical Aspects

Worthy of note in a journal devoted to world medicine is the fact that contributions to the knowledge of tetanus have come from many lands. The results are a credit to the co-operative efforts of the medical profession and allied fields throughout the world. In the most ancient medical records, namely the Edwin Smith Surgical Papyrus, which was written about 1500 B.C. and which according to Breasted, its translator, was copied from a manuscript dating back to 3000 B.C., is found a description of a patient who apparently had tetanus[1]. Hindu and Chinese medical archives carry similar accounts.

Hippocrates, the Grecian physician, is singled out by some medical historians as the first person to make a major contribution in the field of tetanus. The Hippocratic treatises contain observations on patients who had tetanus in its various forms. He was the first to recognize the disease as a distinct clinical entity and to name it, using as a basis the Greek word meaning to stretch.

It was not until the aetiologic significance of contaminated wounds was recognized during the eighteenth century that much new information was added to the knowledge of tetanus. In the next century, specifically in 1884, two Italians, Carle and Rattone, were the first to demonstrate clearly the infectious nature of this disease. Material obtained from an acne pustule beneath the chin of a patient who had just died of tetanus was injected into 12 rabbits; the injections were made into the sciatic sheath in four animals, into the muscle of the back in six and intraspinally in two. All but one rabbit died of tetanus. Injections then were made into four other rabbits, two receiving an emulsion of the sciatic nerves and two receiving blood from the dead rabbits. The first two animals died of tetanus, whereas the other two were unaffected. None of eight control rabbits into which ordinary septic material was injected had tetanus.

Although a German, Nicolaier, is credited with the discovery of *Cl. tetani*, in 1884, the first pure culture was not produced until 1889 by Kitasato, a Japanese, working in Berlin. His success came only after the organism was recognized as an anaerobe. He noted that the organism, when injected into animals, did not spread into the blood stream or the remainder of the body but remained at the site of injection. From these findings, he proposed the theory, which was proved subsequently, that the symptoms of tetanus were the result of a potent toxin produced at the focus of infection. The historical material included in the last three paragraphs has been gleaned from the textbook of Holmes[2].

An interesting temporal relationship exists between the scientific advancements made in diphtheria and in tetanus; important contributions made near the end of the nineteenth century, particularly in prophylaxis, occurred first in diphtheria, and this new knowledge then was applied in tetanus (Table I).

Opportunity and timing have played important roles in history. Fortunate indeed was the association of Kitasato, who was investigating the cause of tetanus, and von Behring, a German investigator, who had just produced prophylactic (toxin-antitoxin) immunization against diphtheria. It was, therefore, only natural for Kitasato, with the help of his illustrious colleague, to duplicate successfully these same results with *Cl. tetani*. Similarly, Ramon, a Frenchman, chose tetanus in an attempt to duplicate the success he had experienced in the development of diphtheria toxoid for immunization. Zoller and Descombey assisted him and together they are credited with the production of tetanus toxoid.

Basic Concepts that are of Clinical Importance

The clinical entity of tetanus is actually a complication of infection with *Cl. tetani*. The latter usually is confined to injuries or wounds, whether large or small. Such infections can and do occur frequently without the development of clinical tetanus. Of utmost importance is the fact that clinical tetanus often follows obscure wounds; many such lesions are so insignificant that the patient does not even consider seeking medical attention. This is one reason why universal active immunization by means of toxoid is so valuable. The availability of passive prophylaxis by use of antitoxin is of no worth if the patient is not seen by the physician. The spores of tetanus probably are capable of remaining latent in a wound, only to be disseminated or activated by subsequent surgical interference or trauma.

The existence of considerable variation among strains of *Cl. tetani* with regard to such factors as toxicity and resistance of spores probably accounts for some of the clinical variability encountered in tetanus. The organism gives rise to two separate exotoxins, both of which possess antigenic properties. The more important of these toxins is tetanospasmin, which is a neurotoxin and which is responsible for the clinical picture of tetanus. The other toxin is tetanolysin, which is a haematoxin.

The neurotoxin of tetanus shows great variation with respect to its effect on various species; man, monkeys, apes and horses are extremely susceptible, whereas cats and dogs are moderately resistant and cold-blooded animals and birds are immune to its effects. Tetanospasmin is one of the most powerful toxic agents known; Abel[3] has estimated that 0·01 mg. of strictly pure toxin constitutes a lethal dose for a 150-pound man. This toxin has a tremendous affinity for the brain and spinal cord of susceptible hosts. This union of toxin and cerebral tissue apparently is in the form of adsorption, as

the linkage can be broken by disintegration of the tissue cells; such disruption leaves the toxin undamaged.

The pathogenesis of tetanus constitutes a realm characterized by a considerable degree of controversy. Definite and pathognomonic pathologic changes in both muscles and nervous system are absent. A number of theories regarding the pathogenesis have been promulgated. Tetanus has been considered as a disease of the central nervous system only, a view that generally has been opposed. Some workers considered that toxin acts directly on muscles in addition to its effects on nervous tissue. Some maintained that it enters the blood stream and then becomes localized in muscle tissue. Many investigators have held to the well-known idea that the toxin of tetanus is transported to the central nervous system by way of the axis cylinders of motor nerves. A variation on this theme is the assumption that tetanospasmin approaches the central nervous system *via* the endoneural and perineural tissue spaces. Others have contended that the toxin is transported from the focus of infection to the central nervous system by way of the arterial blood.

The bulk of evidence tends to indicate that the neurotoxin of tetanus has two independent actions, one directed centrally and one directed peripherally. The central effect results in reflex motor convulsions caused by the toxic effects on the motor nerve cells of the medulla, pons and spinal cord. Spasm of the voluntary muscles is the hallmark of the peripheral effect of the toxin on the motor end organs. Clinical evidence tends to indicate that diffusion of toxin near the site of injury may produce direct local effects on the peripheral nerves in that locality. One of our patients had a badly infected injury of the hand. This patient had received some tetanus antitoxin and was having purely localized clonic spasms of the muscles of the wrist and forearm near the wound. Because of the absence of any other signs of tetanus, use of antitoxin was discontinued. Within 36 hours, the patient showed evidence of full-blown tetanus, with trismus and generalized tonic and clonic spasms. Another patient displayed much more severe tonic contractions in the injured arm than were present elsewhere in the body, the affected arm being in a state of contracture that was relieved by administration of tribromoethanol (avertin). The various theories regarding the pathogenesis of tetanus have been summarized by Drew[4]. It is obvious that no one theory is entirely satisfactory at present.

Another factor of clinical importance is the non-immunizing quality of an active tetanus infection. Often quoted is the observation that the laboratory assistant of von Behring had tetanus on three separate occasions. It is evident that repeated exposure to the causative organism of tetanus does not result in active immunization of the person so exposed. This lack of immunity following tetanus renders it advisable for the physician to urge patients who have recovered from the disease to receive a course of active immunization. This is doubly important in such cases because a number of these patients will have been rendered sensitive to antitoxin during treatment, thus making subsequent prophylactic or therapeutic use of antitoxin somewhat hazardous.

Clinical Aspects of Tetanus

The symptomatology of tetanus is too well known to warrant reiteration in this report. Clinical tetanus becomes apparent only when the afore-mentioned neurotoxin has been produced in sufficient amounts and has combined with those vulnerable components of the nervous system for which an affinity exists. Thus, the diagnosis of tetanus is made by necessity on clinical grounds, for time is important. Bacteriologic cultures are slow and are helpful in only 25 to 50 per cent of cases.

Tetanus has two redeeming features. If the patient survives, tetanus is a self-limited disease; secondly, recovery is usually complete. Regardless of the severity of the diease, the morbidity lasts about three to five weeks. If the patient survives the first 10 days of the disease, the prognosis usually improves daily thereafter. If the patient is still alive after 14 days, the outlook is usually good. There apparently is no way to shorten the course of the illness. Therefore, the aims of the physician should be to prevent the process from progressing and to use every means available to relieve symptoms and maintain vital functions during the disease. Relapses are not common once the patient shows definite and sustained signs of improvement.

Only after the patient has recovered, or nearly so, is the physician able to make an accurate assessment of the severity of the disease. Patients who have tetanus can be classified into four groups. A small number have "severe fulminating tetanus." These patients all die early, usually within two to four days and apparently as the result of overwhelming toxaemia, with early fixation of lethal amounts of neurotoxin to the central nervous system. A larger group of patients have "mild tetanus" during which little more than mild to moderate trismus develops. Present treatment is totally ineffective in the former group and probably is not necessary in the latter group. However, it must be emphasised that, in the early stages of the disease, one cannot predict with any accuracy into which group the patient eventually will be classified.

The remaining large group of patients may be divided into those who have "moderately severe tetanus" and those who have "severe tetanus". Patients in the former group have moderate to severe symptoms but at no time in the course of the disease are their lives endangered. In severe tetanus, the symptoms are serious enough to place the lives of the patients in a precarious state during some stage of the disease. Many of these patients die during the critical stages of the disease. The amount of neurotoxin formed and the extent to which it is combined with the central nervous system probably are the important factors that govern the severity of tetanus. The patients who do not die can be considered as having had less than a lethal dose of toxin combined with the central nervous system. Fortunately, these patients represent the large majority of those who have tetanus. The condition in such patients should be, and usually is, amenable to proper treatment.

General Aspects of Treatment: The Tetanus Team

Knowledge of the previously mentioned basic concepts is particularly important in the treatment of patients who have tetanus. Prompt and skilful care may well influence the prognosis of any given patient. Unfortunately, an effective method of treatment that will reverse the disease process once symptoms are present is not yet available. Tetanus will continue to be one of the most dreaded diseases until means are discovered to disrupt or influence favourably the firm bond between the potent exotoxin and the affected motor cells and nerve fibres.

Since it is impossible to gauge the potential severity of tetanus or know whether a lethal dose of toxin has become fixed in the central nervous system of any patient during the critical phase (first seven to 14 days) of the disease, all patients must be treated when first seen as potential candidates for the more severe forms of the disease. Such an approach may lead in some instances to more intensive and possibly more radical treatment than subsequently would appear necessary, but it is justified in view of the fact that mortality rates from tetanus, even in the best medical centres, range from 20 to 40 per cent. To temporize may jeopardize the life of the patient and decrease the effectiveness of available treatment. Prompt judicious treatment is important and a planned regimen should be in mind for immediate activation when a patient with tetanus is encountered. We should like to outline the plan of treatment now being used at the Mayo Clinic.

The Tetanus Team

The team approach in the management of tetanus is logical and is to be encouraged. Clinical evidence supports the contention that this is the most effective method in dealing with the problem. Spaeth[8] reported that centralization of control in a specially trained medical and nursing staff at the Cook County Hospital, in Chicago, appeared pertinent in the reduction of the mortality rate from 65 per cent in 180 patients prior to such centralization to 35 per cent in 96 patients after its establishment. Our experience at the Mayo Clinic supports this impression. Prior to installation of a team approach in the treatment of tetanus in 1946, the mortality rate at the clinic was 52 per cent in 66 patients, whereas the mortality rate since inception of this programme has decreased to 27 per cent in 26 patients[9]. This significant decrease in the mortality rate has been attributed not to any new treatment but to the presence of the tetanus team. Such an approach allows greater utilization of the available measures and methods.

Ideally, the team should consist of physicians whose specialties might contribute to the problem of tetanus in all of its various facets. The size of the team is determined by the number of specialists interested and available. At the clinic, the tetanus team consists of three internists, two neurologists, two orthopaedists, two anaesthesiologists, a paediatrician, two plastic surgeons, a clinical pathologist, two bacttriologists, a clinical physiologist and a pharmacologist. Specialties represented by more than one physician are those in which it is important that at least one of its representatives be available when a patient with tetanus is encountered. It is important to have one member designated as the co-ordinator to direct the activities of the team and the care of the patient. An internist acts in this capacity at the clinic. It is the responsibility of the various members of the team to keep well informed concerning the most modern and effective methods of treatment and to be available to help. A competent and experienced nursing staff is an important component in the team approach.

Table 1—Temporal Relationships in Immunologic Developments in Diphtheria and Tetanus

Diphtheria	Tetanus
1883: *Corynebacterium diphtheriae* discovered by Klebs (Germany)	1884: *Clostridium tetani* discovered by Nicolaier (Germany)
1888: Extracellular toxin shown to cause symptoms and death by Roux and Yersin (France)	1889: First pure culture: Kitasato suggested symptoms due to exotoxin (Germany)
1890 (Early): Toxin-anti toxin immunity first produced by von Behring (Germany)	1890 (Later): Toxin-antitoxin immunity first produced by von Behring and Kitasato (Germany)
1922-1924: Diphtheria toxoid first produced by Ramon (France)	1924-1927: Tetanus toxoid first produced by Ramon, Zoller and Descombey (France) and shown to produce active immunity.

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PART TWO

Care of the Patient

Patients who have tetanus or who are suspected of having the disease should be hospitalized, thus insuring close supervision and good nursing care. Special nursing care is a necessity in patients who have moderately severe or severe disease until they are out of

danger. Treatment in the initial phase consists of measures that will prevent any further fixation of tetanus exotoxin to nervous tissue, with elimination of any foci of infection that might harbour the causative organism. As previously noted, the clinical features of tetanus follow involvement of the vulnerable nervous system, and when such changes are irreversible it is important to combat early the potential threat of the disease as well as to alleviate its symptoms.

Use of Antitoxin

Tetanus antitoxin has a specific affinity for the toxin if these two agents are brought into contact prior to fixation of the latter to nervous tissue. No amount of antitoxin or any other measure now available will disengage this bond or prevent the disease from developing once the toxin has become fixed. Thus, the earliest symptoms, regardless of severity, signify that this union of neurotoxin and nervous tissue has occurred.

Adequate methods do not exist at present to determine the amount of toxin that has been produced in a patient at any given time, the amount circulating in the body fluids or the amount already combined with the nervous system. Therefore, it is impossible to know in advance what constitutes an adequate dose of antitoxin for any given patient and to anticipate the value of such therapy in that patient. Although the method of treatment of tetanus is fairly well standardized, the dosage of tetanus antitoxin at present is individualized and dependent on presenting circumstances, as judged by the physician.

As soon as is feasible after the clinical diagnosis has been made, the patient should be given tetanus antitoxin in quantities that are estimated to be adequate to neutralize any circulating or uncombined toxin and any that will be produced prior to elimination of the focus of infection. In the absence of any method to determine that amount and after testing for hypersensitivity, we arbitrarily give 15,000 to 50,000 units intravenously or 10,000 to 30,000 units intramuscularly or both. Smaller amounts are used if the wounds are small and superficial than if they are deep, penetrating and badly infected. Larger amounts are given if the symptoms are well advanced or are progressing rapidly to suggest an overwhelming infection. Smaller amounts of serum are then given during the next few days until the focus of infection has been removed and the disease process stabilized. Once this has occurred, it can be assumed that maximal benefit has been derived from tetanus antitoxin. Intrathecal administration of the antitoxin is unnecessary and, when dangerous, should be discouraged.

As already indicated, the use of tetanus antitoxin in either horse or beef serum must be preceded by the usual tests for sensitivity and the team must be prepared to treat adequately the various potential hazards associated with "foreign-protein" therapy. The most feared hazard, of course, is the anaphylactic reaction. Fortunately, this is rare. Ampoules of 1:1,000 solution of epinephrine, needles and syringes, a 5 per cent solution of dextrose for intravenous use, antihistamines and l-arterenol should be on hand, along with a tourniquet, an oxygen tank and mask, and ampoules of corticotropin (ACTH) or hydrocortisone. The use of diphenhydramine hydrochloride (Benadryl) or tripelennamine hydrochloride (pyribenzamine) in doses of 25 to 100 mg., depending on the patient's age, is recommended to help prevent or suppress mild or delayed serum reactions. These drugs also aid in sedation. Both are given by mouth but the former can be used parenterally if necessary.

Sedation

The amount and kind of sedative drug used also depend on the individual needs of the patient. Enough is that amount which will keep the patient reasonably comfortable and allow periods of restful sleep. It is unnecessary, even dangerous, to keep the patient under deep or prolonged narcosis. Barbiturates, chloral hydrate, bromides or paraldehyde may be used to control mild or moderately severe tetanospasm.

Depending on the age of the patient and the severity of the disease, tribromoethanol (avertin) in doses of 50 to 70 mg. per kilogram of body weight has been used in a rectal retention enema; in our opinion, avertin given in this fashion is the drug of choice for the sedative control of severe tetanospasm. Restful sleep for 3 to 6 hours usually supervenes and, on awakening, the patient frequently is sufficiently relaxed so that he can take food and fluids with the help of the nurse without too much difficulty. One or two administrations of avertin per 24 hours usually suffice but occasionally three enemas are necessary. Except for proctitis in one patient, side effects as reactions have been minor and few in our experience.

Morphine sulphate, curare or other respiratory depressants have a low margin of safety, and other medications that will produce the same desired effects with a greater margin of safety are preferable. Magnesium sulphate given by injection is of questionable value and is likewise dangerous. Codeine and meperidine (demerol) hydrochloride, unlike morphine, are useful adjuncts in the management of tetanus. They are used as necessary to control pain, and their administration often lessens the frequency with which avertin has to be given. We have had no experience with the newer tranquilizing group of drugs. Adriani and Kerr[1] gave a combination of mephenesin and chlorpromazine to 11 patients; they considered chlorpromazine as a valuable adjunct because of its enhancing action on other drugs, such as barbiturates and mephenesin, without the production of circulatory or respiratory depression. It apparently did not alter favourably the mortality rate.

Antibiotics

Penicillin and dihydrostreptomycin in daily doses of 1,000,000 to 2,000,000 units and 1 to 2 g., respectively, in adults, are as effective as any antibiotic therapy available at present in combating *Cl. tetani* and symbiotic organisms; proportionately smaller doses are used for children. The use of antibiotics affects the course of the disease only in helping to eradicate foci of infection. thus preventing production of more exotoxin. However, even larger doses of antibiotics cannot be completely

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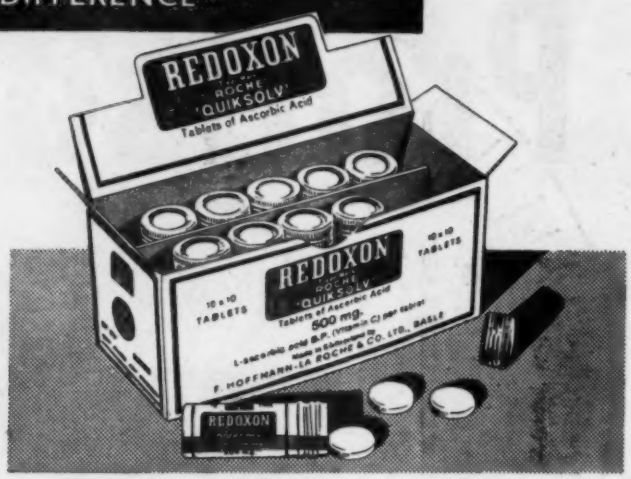

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relied on to do this, particularly if the wounds are deep and badly infected. Clostridial organisms are true anaerobes and thrive in dead or dying tissue, in which the blood supply is reduced or absent. Administration of antibiotics should be continued until the focus of infection has been eliminated. It is also of value in the prevention or treatment of pneumonia and other intercurrent infections, which are prone to develop in cases of severe tetanus.

Care of Wounds

When administration of tetanus antitoxin and antibiotics has been started, adequate debridement and other care of the wound should be accomplished. As mentioned previously, lethal doses of toxin can be produced in trivial wounds. Too often the natural tendency is to be too conservative in the treatment of these foci. Deferment of debridement of wounds may put the patient's life in serious danger. Amputation of a finger or, if necessary, an extremity, or hysterectomy should be done if the focus cannot otherwise be handled safely and adequately. Tetanus is a serious disease in which every precaution must be taken if the patient is to receive his maximal chance for survival. In no other disease is good medical and surgical judgment any more important.

When amputation, hysterectomy, extensive debridement or other such surgical procedures become necessary, general anaesthesia is effected best by the intravenous administration of thiopental (pentothal) sodium or the rectal administration of avertin. Ether is irritating to the respiratory tract, tending to increase tracheobronchial secretions or laryngospasm or both, thus aggravating the patient's condition and, in time, predisposing him to pneumonia. If use of an oxidizing agent is indicated, dressings moistened with potassium dichromate or potassium permanganate are better than hydrogen peroxide dressings, which frequently cause cutaneous irritation.

Tracheotomy

Tracheotomy should be done in tetanus whenever respiration is sufficiently embarrassed by laryngospasm or the accumulation of tracheobronchial secretions. Experienced surgeons can perform this procedure quickly and usually with minimal risk with the aid of pentothal or avertin to induce general anaesthesia. This can be done in the operating room while the wounds or injuries are being treated or, if necessary, in the patient's room. Tracheotomy has been a lifesaving procedure in many patients with tetanus; and it should be performed early rather than late in the course of the disease. During the critical period of the first 7 to 14 days of infection, it is advisable to have an emergency surgical tracheotomy set in the rooms of all patients who have tetanus of more than mild degree.

Diet

The diet must be adequate in calories, vitamins, proteins and electrolytes. It should be prepared in the manner best tolerated by the individual patient. When tetanus is mild, a general soft diet usually suffices. When symptoms are moderately severe or severe, a high-caloric diet adequate in vitamins and proteins is indicated when metabolism is greatly increased. Liquid to soft foods are tolerated better than solids when trismus and dysphagia are present. These patients frequently need the help of a nurse to feed them, and multiple small feedings are better tolerated than are three large meals. Food should be given when the patient is most relaxed and able to swallow. As mentioned previously, an opportune time often follows a period of induced rest. The nurse should use special care to avoid aspiration by the patient of food or liquids into the lower portion of the respiratory tract. The required intake of fluid in these patients frequently is increased because of excessive perspiration, increased metabolism and, at times, fever.

A gastric tube passed intranasally should be used when necessary and when it does not aggravate the condition unduly. Supplementary fluids containing dextrose, proteins, electrolytes and vitamins are given parenterally as needed to maintain adequate hydration, nutrition and electrolytic balance.

Hormonal Therapy

The adrenocortical and adrenocorticotropic hormones are used only when tetanus or its associated complications warrant this form of treatment. Contraindications are the same as in any other disease of a similar nature. We do not use these steroids in the treatment of the less severe uncomplicated forms of tetanus. The patients to whom these hormonal agents are given comprise three main groups: (1) patients known to be sensitive to tetanus antitoxin or who experience reactions to serum during its use; (2) patients in whom some other serious intercurrent infectious disease, such as pneumonia or micrococcal enteritis, develops during the course of tetanus (this group includes instances of tetanus in drug addicts, in whom this disease is especially severe); (3) patients who have severe tetanus and who show signs of exhaustion and reduction in their total reserve as the result of the stress of severe tetanospasms.

In the first group, hormonal therapy, along with antihistaminics and other antiallergic measures, is given to suppress or counteract allergic manifestations due to antitoxin so as to allow use of antitoxin as indicated. In the second and third groups of patients, adrenocortical hormones are preferred to the adrenocorticotropic agents when the integrity of the adrenal gland may be in question. In these two groups, cortisone or hydrocortisone serves in a supportive role to supplement the total programme of treatment in an effort to sustain the life of the patient while he is passing through the crisis of this self-limited disease. Depending on the age, sex and condition of the patient, and in the absence of absolute contra-indications, 100 to 200 mg. of cortisone or hydrocortisone is given each day in divided doses until the crisis has passed. Thereafter, doses are reduced and use of the preparation is discontinued gradually.

Rarely is it necessary to continue use of steroid agents more than 2 to 3 weeks and, therefore, significant side effects have been uncommon. Oral administration is preferred but some of the agents can be given parenterally if necessary. These hormones do not alter the underlying disease process or the duration of the

disease but are given to enhance the patient's ability to cope with the disease and its complications as already indicated. Opinions regarding the value of steroid agents in the treatment of tetanus are still in the formative stage.

Other Symptomatic and Supportive Measures

Oxygen should be administered whenever indicated. A portable respirator proved useful to one of our patients in maintaining respiratory function when heavy sedation was necessary to control tetanospasm and when he was in the exhaustive phase of the illness.

We have not tried hypothermia in the treatment of patients who have tetanus, nor have we been encouraged to do so by the results published by those who have used this form of therapy.

Urinary retention should be recognized early and relieved by catheterization.

Immunization Against Tetanus

The previous sections of this paper have made apparent the manifold problems that arise when treatment is necessary because clinical tetanus has developed. The obvious way to dispel these problems is to prevent the appearance of tetanus by passive or active immunization.

Passive Immunization—Little need be said here regarding passive immunization by the injection of tetanus antitoxin at the time of injury. It is a controversial field in which the circumstances of injury and the physician's judgment play a large part in the final decision as to whether it should be given.

Naturally, a person who has a tetanus-prone injury and who has not had previous active immunization should receive a prophylactic dose of tetanus antitoxin after appropriate preliminary skin testing to determine the possible presence of sensitivity. For many years the accepted average prophylactic dose of antitoxin was 1,500 units. Modern serums are more purified and concentrated than were the older preparations; consequently, many physicians now give 3,000 units or more, depending on circumstances. For injuries occurring in barnyards for example, as much as 10,000 units or more may be used prophylactically.

Active Immunization—Administration of tetanus toxoid to produce active immunity apparently results in a much greater degree of protection than does injection of antitoxin. The use of peptones has been eliminated in the modern preparation of these toxoids and, as a consequence, reactions after their use are extremely minimal. Adequate evidence exists that most persons will exhibit a protective level of tetanus antitoxin in their blood (more than 0·1 unit per millilitre) within 2 or 3 weeks after the second dose of alum-precipitated toxoid or after the third dose of fluid toxoid.

A subsequent "booster dose" given 6 months to a year later then produces a far greater increase in circulating antitoxin within 2 or 3 weeks. It is preferable not to consider this first injection after the completion of the "primary" immunization as a booster dose; rather, it should be regarded as an integral and a fundamental part of the original immunization procedure. The high levels of antitoxin so induced are sustained for long periods, and subsequent booster doses result in increasingly greater responses.

Immunization Schedules—Two forms of tetanus toxoid are in common use. The fluid toxoid usually is given in three doses of 1 ml. each, administered subcutaneously 2 or 3 weeks apart. A subsequent dose then is given 6 months to a year later. The second type of toxoid is the alum-precipitated form. This usually is given in two doses of either 0·5 ml. or 1 ml. at an interval of 4 to 6 weeks, with a subsequent dose given 6 months to a year later. With either preparation, booster doses should be given at the time of any injuries that might be conducive to the development of tetanus. Present custom also is to give regular booster doses at intervals of 3 to 5 years. This time interval is somewhat arbitrary and may be shorter than is actually necessary.

Comment—The efficacy of active immunization against tetanus by use of toxoid has been proved by the experience with United States military personnel during World War II. A total of 2,800,000 soldiers and sailors were wounded during this war, yet only 16 cases of tetanus were encountered. Active immunization had not been given to six of the 12 soldiers who got tetanus. Complete confidence was placed in the active immunization induced by toxoid, in that antitoxin was not given to any wounded soldier or sailor except in the event of doubt as to whether a complete course of toxoid had been received previously.

The afore-mentioned schedules of immunization, namely a primary series of injections, a subsequent dose 6 months to a year later, and periodic booster doses thereafter are sufficient to maintain protective levels of antibodies for 2 to 5 years, or perhaps more; after the last dose, in most cases. Because of individual variations in the rate of decrease of antitoxin after booster doses, it is impossible to predict with certainty the precise duration of adequate protection in any given person. Thus, the consensus at present in the United States reflects the custom that periodic booster injections should be administered every 3 to 5 years. However, evidence is accumulating gradually as years go by to indicate that a booster dose of toxoid given at the time of injury will call forth adequate protective responses even though the last previous injection of toxoid may have been given 6 to 8 years or more earlier.

Injection of a booster dose of tetanus toxoid in an actively immunized person results in a significant increase in the amount of circulating antitoxin within 4 or 5 days; occasionally, an appreciable response is not evident for 7 days. Boosters of fluid toxoid ordinarily induce a quicker response than does use of the precipitated prepartion. The response apparently is slower when the last previous dose of toxoid has been given more than 4 years previously. Thus, a period of non-protection of several days theoretically could be present during which fulminating tetanus could develop before the body's defence mechanism comes into operation. Therefore, a minority of investigators still advise prophylactic use of antitoxin after a wound or burn even in persons who have been subjected to an adequate

programme of active immunization. However, the aforementioned efficacy of active immunization as reflected in the experience during World War II lends force to the general opinion that use of antitoxin is not needed to supplement administration of a booster dose of toxoid, preferably the fluid form at the time of injury.

Another vexing and controversial problem is the question regarding the efficacy of toxoid given to start the induction of active immunity at the same time that antitoxin is administered for prophylactic purposes in a nonimmunized person. Earlier experimental work appeared to indicate that the presence of circulating antitoxin interfered with the production of active immunity by the injection of toxoid. It was shown by Gold and Bachers[3] that simultaneous administration of toxoid and 1,500 units of tetanus antitoxin produced only partial diminution of the immunizing power of toxoid in humans. However, the use of doses as large as 10,000 or more units of antitoxin apparently can suppress entirely the antigenic qualities of simultaneously given toxoid[3]. Under such circumstances, the initial injection of toxoid should be delayed for 6 weeks or so until the amount of circulating antitoxin has decreased to nonsuppressive levels.

It is obvious that universal active immunization by means of tetanus toxoid, with complete reliance on subsequent booster injections of toxoid instead of prophylactic use of antitoxin, would resolve many of the problems to which reference has been made. Edsall[4] has summarized the situation with the statement that, "It is the physician's responsibility to see that each of his patients is adequately immunized with tetanus toxoid before the emergency occurs. If this is properly done, the dilemma of simultaneous active-passive immunization need not arise, and the use of antitoxin with its discomforts and dangers can be obviated".

Summary

Tetanus is a disease of world-wide distribution that will continue to plague mankind until active immunization against it is applied universally. The clinical entity of tetanus is a complication of infection with *Clostridium tetani*, as the symptoms are produced by the toxin elaborated by the organisms, which remain at the site of injury.

Immunity to further attacks is not conferred on the person who has recovered from tetanus. Severe tetanus can follow such obscure and unimportant wounds that the person does not think of seeking medical attention for them. The diagnosis of tetanus rests on clinical grounds, as speed in beginning treatment is of utmost importance.

The main purposes in the treatment of tetanus are to prevent the combination of a lethal dose of toxin with the nervous system and to provide supportive measures so that the patient does not die from exhaustion or other complications of the disease. The use of a tetanus team for the management of patients who have this disease can produce a significant reduction in the mortality rate. Specialists who may be included on such a team are internists, neurologists, orthopaedists, anaesthesiologists paediatricians, plastic surgeons, clinical pathologists, bacteriologists, physiologists and pharmacologists.

The care of the patient with tetanus includes early and vigorous use of adequate amounts of antitoxin, surgical care of the wound, use of sedative agents and antibiotics, tracheotomy if needed, an adequate diet, use of oxygen and parenteral administration of fluids and electrolytes. Adrenocortical and adrenocorticotropic hormones may be needed on occasions.

The problems inherent in the treatment of clinical tetanus can be obviated by universal active immunization through injection of tetanus toxoid. Physicians must assume the responsibility of having their patients receive such active immunization to prevent the emergency situations presented by the development of clinical tetanus.

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NOTES AND NEWS

W.H.O. Regional Body Meeting

The tenth annual session of the World Health Organisation's Regional Committee for South-East Asia was held in Rangoon from September 16 to 21. Delegates from Afghanistan, Burma, Ceylon, India, Indonesia, Nepal, Portugal, Thailand and the U.K. attended the session, in addition to representatives of the U.N., U.N.I.C.E.F., F.A.O. and the U.N.

More U.N. Aid for Tuberculosis Control in India

Additional assistance to the National Tuberculosis Control Programme in India, has been recommended by the executive director of the U. N. Children's Funds. Continuing assistance to the national B.C.G. anti-tuberculosis vaccination campaign has also been recommended.

Under this, U.N.I.C.E.F. would provide India equipment for three mobile treatment units and for one mobile survey unit which are to begin operations in 1958 as essential parts of the new national tuberculosis control programmes. U.N.I.C.E.F. would also provide vehicles to replace those provided earlier for the B.C.G. campaign, which will not be serviceable beyond 1958.

The allocations recommended to India total $196,000 while the Government of India expenditure matching them totals $928,000.

The Government of India's proposals for a National Tuberculosis Control Programme as a part of its Second Plan were presented to the U.N.I.C.E.F. Board last April. The allocation approved by the Board at that time provided equipment and transport for the training aspects of the programme to be implemented in 1958, including a national tuberculosis training centre and three State level tuberculosis training and control centres.

The present allocations recommended would be supplementary to what was approved in April.

More Beds for Tuberculous Patients in Delhi

The number of beds for the treatment of tuberculous patients in Delhi is proposed to be increased by 322 at a cost of Rs. 15·59 lakhs. Additional beds would be provided in the Silver Jubilee Hospital, Delhi, and the Lala Ram Swarup T.B. Hospital, Mehrauli.

It was proposed to establish six T.B. clinics at Shahdara, Paharganj, Pusa Road, Roop Nagar, Nizammuddin and Moti Nagar during the second Five-Year Plan period at an estimated cost of Rs. 27·67 lakhs. It was also proposed to set up an after-care and rehabilitation centre at New Delhi at an estimated cost of Rs. 4 lakhs to provide facilities for teaching T.B. patients and their families suitable handicrafts. The offer of the Care and After-care Committee to place in the hands of Delhi Administration an amount of Rs. 1 lakh for additional beds for T.B. patients was under the consideration of that Administration.

U.N.I.C.E.F.'s Grants to India

The U.N. Children's Fund (U.N.I.C.E.F.) Executive Board approved a sum of $2,123,000 for U.N.I.C.E.F. programmes in India, according to a U.N. Press release on 16 September, 1957.

The programme is mainly concerned with the development of rural health services, with priority for areas under the community development plan. The allocation of $1,546,000 proposed for this programme would provide equipment and supplies to 250 primary health centres and 750 subcentres, 80 hospitals and 70 laboratories; sanitary equipment for 2,200 schools; and vehicles and equipment to improve the health administration in approximately 75 districts. All 14 States will benefit under this programme being carried out in conjunction with the community development programme.

The next largest allocation involves $330,000 for a municipal milk scheme in Ahmedabad. U.N.I.C.E.F is asked to equip a new dairy with six milk collection units, tankers for milk transport in bulk and trucks and carriers for the local distribution of milk.

The third allocation of $96,000 is for the continuation of anti-TB programmes in India. India has an estimated 2·5 million active cases of TB and 500,000 TB deaths every year.

The fourth item, the expansion and improvement of the teaching in treatment of children's diseases at the Osmania Medical College in Hyderabad, has an allocation of $46,000. U.N.I.C.E.F. is asked to provide technical equipment and supplies to four hospitals and six child-health units, and fellowships and stipends for various national personnel engaged in paediatric services or training.

Finally $5,000 have been allocated for eight fellowships for nurses to study paediatric nursing at the Paediatric Department of Madras Medical College.

Child Health Project

The paediatrics centre in Hyderabad, one of the five to be established in India, is to be opened at Niloufer Hospital for Women and Children shortly, by the State Government with financial assistance from the Government of India and aid from the World Health Organisation and the United Nations International Children's Emergency Fund.

Plans for the construction of an up-to-date paediatrics ward with a separate out-patient department, laboratory facilities, etc., are being got ready at a cost of about Rs. 3 lakhs.

The establishment of the centre had been included in the general schemes of upgrading the Osmania Medical College and the Osmania General Hospital, for which a Plan provision of Rs. 51·40 lakhs had been made. At present, there are only 250 beds in the Niloufer Hospital, 150 for paediatric and 100 for maternity cases. The bed-strength is proposed to be increased to 250 paediatric (200 medical and 50 surgical) cases. The centre is expected to be declared open by the Union Health Minister in about two months' time.

The Niloufer Hospital for Women and Children was built in 1953 at a cost of about Rs. 22 lakhs and the number of patients attending the hospital daily on an average is 650 at the out-patient and 93 at the in-patient departments.

It was proposed to upgrade the children's out-patient department in the hospital with a view to converting it later into a central consultative clinic.

All the medical-paediatric beds in the Osmania General Hospital had been transferred to the Niloufer Hospital and 35 to 40 surgical beds would be transferred shortly. The staff had also been strengthened. The maternity and child health project had already been implemented in Hyderabad and there was also a network of primary health centres. The maternity and child welfare centres in and around the city would serve as paediatric clinics and as field practice centres for undergraduates. There would be adequate training facilities for the undergraduates and the postgraduate medical personnel. A diploma course in child health would also be opened. Training of auxiliary-nurse midwives, health visitors and nurses would also be undertaken at the centre. The laboratory would be suitably upgraded.

An inspection team from the College of Physicians and Surgeons, Bombay, which recently visited the Niloufer and the I. R. M. Hospital, Secunderabad, had recommended them as training centres for D.C.H. and

D.G.O. examinations. The Royal College of Physicians and Surgeons, London, has also recognised the Niloufer Hospital for post-graduate training.

The Growing Family of Man

According to the 1956 issue of the United Nations Statistical Yearbook by mid-1955, the population of the entire world was estimated at about 2,691 million against 2,246 million in 1940, 2,013 million in 1930 and 1,810 million in 1920.

Rather more than half of all the people live in Asia (excluding the USSR). Europe (excluding USSR) is easily the most densely populated and Oceania the least densely populated continent. The continental distribution of the estimated mid-1955 population and the corresponding population density are shown as follows:

	Population (in millions)	Population per sq. km.
World	2,691	20
Africa	223	7
America (North and South) ...	366	9
Asia (excl. USSR)	1,481	55
Europe (excl. USSR) ...	409	83
Oceania	14·6	2

(1 square kilometre = 0·386 square mile).

According to the latest data given in the Yearbook (generally for the crop year 1954-55 or 1955-56), available supplies of foodstuffs at the retail level represented more than 3,000 calories per head per day in the following countries (arranged in alphabetical order); Australia. Canada, Denmark, Finland, Iceland, Ireland, New Zealand, Norway, Sweden, Switzerland, United Kingdom and United States.

In Belgium, Luxembourg, Netherlands and West Germany available daily supplies of calories per head were close to the 3,000 figure and exceeded 2,800 in the Argentine, Austria, France and Urugnay.

At the other end of the scale, available daily calories per head fell short of 2,000 in Burma (1947-48), Ceylon and India and barely exceeded the 2,000 mark in Honduras, Pakistan and Japan.

The Statistical Yearbook provides data on the number of physicians, dentists, midwives and pharmacists in more than 180 countries.

Thus, for example, in 1954 or 1955, the number of inhabitants per physician—a convenient yardstick to measure medical attention among the more advanced countries was only 630 in Austria, 700 in Switzerland, 720 in New Zealand, 740 in West Germany, 760 in the United States and around 1,000 in most European countries.

Among the less developed countries there was only one physician for 81,000 inhabitants in the Sudan, for 71,000 in Indonesia, for 57,000 in Nigeria, for 18,000 in the Gold Coast and for 9,700 in Kenya.

This eighth issue of the UN Statistical Yearbook was prepared by the Statistical Office of the United Nations with the active co-operation of the statistical authorities of more than 150 countries and territories and with the assistance of the United Nations specialised agencies and other intergovernmental bodies.

Congo Apes Get Live Polio Virus

Strains of the live type of antipoliomyelitis vaccine from the United States are being tried out on a colony of captive chimpanzees in Lindi, 70 miles west of Stanleyville, Belgian Congo. The new project is being sponsored by the Medical Department of the Belgian Congo and Hilary Koprowski of the Wistar Institute, Philadelphia, Pa.

All chimpanzees in the colony are vaccinated with a living, nonvirulent type of one or more strains of the three types of poliomyelitis. About 2 or 3 months later the animals are inoculated with a virulent type of virus. Using graduated doses of the vaccine, the researchers are able to record both reactions and the minimum amount of vaccine necessary for immunity.

Meanwhile, the Health Department of the Congo is investigating the incidence of the disease among isolated indigenous tribesmen. Officials say that poliomyelitis is not a disease of civilization, as usually stated. (*Science*, 19 July 1957).

Indian Scholarships for Foreign Students

To promote cultural relations between India and foreign countries, the Government of India will award 140 scholarships to non-Indian students and students of Indian origin permanently domiciled in 50 foreign countries. The scholarships will be available for higher studies in India under the General Cultural Scholarships Scheme, 1958-59.

The awards will be made for studies in arts and humanities, sciences, agriculture, medicine, technology, education, law, commerce, forestry, veterinary science, engineering, and so forth, subject to the availability of seats in the various institutions in India. Preference will be given to postgraduate students. Recipients will be encouraged to learn at least one of the Indian languages, particularly Hindi.

The stipend has been set at 200 rupees per month. Students must pay their own travel expenses.

Applications for these scholarships are being invited by Indian Government representatives abroad, and scholarships will be awarded on their recommendations. All applications should, therefore, be made to appropriate authorities.

Adequate Medical Relief for People

The Union Health Minister addressing a meeting of the Delhi Medical Association on 10 September, 1957 referred to the present unsatisfactory conditions in the medical profession and the absence of adequate co-operation among the different units of health services. Every hospital should function as a dynamic institution and not as a static body, with the co-operation of all medical men for mutual benefit and a common cause.

The Government, he said, should be enabled to canalise all resources for giving medical relief and thus bring about a welfare State by alleviating the suffer-

ings of the people. A large part of such functions, he suggested, should be entrusted to popular bodies like the Delhi Medical Association (Delhi State Branch of I.M.A.). In order to provide medical relief in an organised way, it was imperative on the part of the medical profession to share equally the Government's responsibility for providing medical aid to the people.

West Bengal Medical Council

1. CORRECT ADDRESSES IN THE MEDICAL REGISTER

The West Bengal Medical Council are trying to make the Medical Register up-to-date in all the particulars recorded therein. It is essential in the interest of the registered practitioners whose names are borne on the Register that their correct addresses should be recorded therein. The Indian Medical Council Act, 1956, would be coming into force soon, and that makes it all the more urgent for the purpose of election to the Indian Medical Council.

Recently the Council sent out about 8,000 letters to registered practitioners in whose cases there was doubt as to the correctness of the addresses recorded with this Council, and many of them have already replied. All registered medical practitioners are requested to intimate to the West Bengal Medical Council (8, Lyons Range, 3rd floor, Calcutta-1) where there has been any change in address, stating their full names with registration number. Those who have already replied to the Council's letter, or have recently intimated their addresses, need not do so again.

Additional qualifications since acquired may also be registered as per rules.

2. CHANGES IN ETHICAL RULES

For Section 3 under Part III of the Ethical Rules, (Information pamphlet) the following shall be substituted :

"3. No member should meet in consultation any practitioner who does not hold a qualification registrable in West Bengal under the Bengal Medical Act or whose name has been removed from the Register by order of the Council for infamous conduct in a professional respect.

"No member should join the teaching staff and participate in teaching any professional subject in an institution not teaching medicine as defined under the Bengal Medical Act.

"This section does not apply so as to restrict the teaching of pre-clinical subjects such as Anatomy and Physiology by registered practitioners in institutions recognised by the Ayurvedic State Medical Faculty of West Bengal and the General Council and State Medical Faculty of Homoeopathic Medicine of West Bengal, and in other non-medical teaching institutions.

"There is no objection to a registered practitioner seeing a patient even if already attended by an unqualified practitioner, so long as he gives his advice to the patient directly and does not enter into consultation with the unqualified practitioner."

Indian Nursing Council Act

The Union Health Minister introduced on 14 September 1957, in the Rajya Sabha a Bill to amend the Indian Nursing Council Act, 1947.

According to the statement of objects and reasons, the Bill is designed to extend the Nursing Council Act to the whole of India except the State of Jammu and Kashmir, to make certain changes in the constitution of the Council and to facilitate the registration of Indian citizens holding foreign qualifications and the temporary registration of foreign nurses who are engaged as nurses or teachers or administrators in hospitals or institutions in India.

The Bill also seeks to empower the Central Government to amend the schedule listing recognised qualifications and to provide for the maintenance of an all-India register of nurses.

CORRESPONDENCE

The Editor is not responsible for the views expressed by correspondents

"Doctors for Rural Areas"

SIR,—I have read a letter by Dr. P. K. Chatterjee of Calcutta in the columns of your journal dated July 16, 1957 under the caption "Doctors for Rural Areas".

I quite agree with Shree P. C. Mahalanobis, a member of the Planning Commission, when he pleads for reintroduction of a short term training for doctors. But my slogan is "half trained doctors for ill-equipped and ill-staffed dispensaries wherever they may be situated" rather than "half trained doctors for rural dispensaries".

It is common knowledge that the performance of a doctor is directly linked with the equipment and staffing of his hospital. A surgeon or physician with high academic qualifications who does wonders in the premises of the highly equipped medical colleges will have to behave just as an ordinary doctor if put in charge of a dispensary where the equipment and supply of medicine are just marginal and everything is a one-man show.

It was a bad day when the decision of abolishing the Licentiate Course was taken. Today hundreds of medical graduates are rushing to ill-equipped dispensaries where in spite of their better training they are not able to do anything more than their Licentiate predecessors. When the same graduate is placed in a well-equipped and well-staffed hospital he does quite well and proves to be an asset for the institution.

Can there by any justification to put a medical graduate in charge of a dispensary where the work is limited to distributing common mixtures and tablets, incising abscesses and extracting loose teeth?

I will appeal to the Indian Medical Association to review the matter seriously and make an amendment to their prior decision of having only one caste of doctors. If they go on a fact-finding mission I may say, at least about Bihar, that they will see how the

training of a medical graduate is being wasted when he is made in-charge of a poorly equipped and a mobile dispensary and of a dispensary situated in a backward area where there are only few people to attend the hospital and understand what is scientific treatment.

This is also a fact that the Licentiate brother fits in the rural society in a much more nice manner than his graduate counterpart.

I am etc.

Thethaitangar (Ranchi). S. P. SRIVASTAV, M.B.B.S.

REVIEWS

Lumbar Puncture and Spinal Analgesia—By Sir Robert Macintosh, M.A., D.M., F.R.C.S. (EDIN.), F.F.A.R.C.S. Second edition, 1957. Board-bound, 9"×6", 142 pages with 111 illustrations. E. & S. Livingstone Ltd., Edinburgh and London, U.K. Price 25s. net, regd. postage 1s. 5d.

First published in 1951, this book has seen a German and Spanish edition in 1953 before appearing in this second edition. An excellent book on the subject, this should be thoroughly read and assimilated by all who want to perform lumbar punctures and specially, give spinal anaesthetics. It has indeed been rightly said that "the apparent simplicity of the monoeuvre constitutes its greatest danger in the hands of the tyro." The large number of illustrations and instructive practical details will be highly appreciated by those embarking on spinal anaesthetic procedures for the first time, and will be constantly useful to persons who administer spinal anaesthetics quite often.

Indian Armed Forces in World War II—Medical Services—Medicine, Surgery and Pathology.—Edited by B. L. Raina, LT.-COL., A.M.C. Published 1955 by the Combined Inter Services Historical Section, India and Pakistan (Director—Bisheshwar Prasad, D.LITT.). Board bound 10"×7", 906 pages, price Rs. 40/-.

After the termination of the second World War, the Historical Section was established in 1946 for the purpose of recording the part played by the armed forces of pre-partition India in the various theatres of the second World War. Even after the partition of India, the two Dominions, India and Pakistan, agreed to maintain this Historical Section as a joint organisation. It has thus been possible to publish these volumes of the medical series edited by Lt. Col. B. L. Raina. This present volume is the second in the medical series of the Official History of the Indian Armed Forces in the Second World War, dealing with medicine, surgery and allied subjects, based mainly on the observations made and the experiences gained in the eastern theatre, as also on the researches conducted in important diseases encountered in Burma and South-East Asia. Only those diseases and disorders are naturally mentioned here which had led to a relatively large number of casualties or those which assumed special importance. The material presented in this volume may be very usefully supplemented by the accounts published during and after the war, particularly the volumes prepared by U.S.A. and the Commonwealth countries—specially the six volumes of *Bulletin of War Medicine* of the Medical Research Council in London. The eastern theatre of war, the area covered in this volume proved the truth of the statement that although popular attention finds its chief interest in the number of wounded and dead, yet the inefficiency from disease in every war has out-numbered many times the losses from killed or wounded. For one soldier wounded in the Indo-Burma front, 204 were sick in 1942 and 142 in 1943 with the ratio of battle and non-battle casualties reduced to 1:13 by 1945. The Indian Army employed only 87 specialists at the outbreak of war while, by August 1945, the number increased to 1,576. Similarly, the hospital beds increased from 12,821 in 1939 to 169,981 in 1945, with over 5 million of cases having been treated in these hospitals. These are just a few interesting data. A careful perusal of the account contained in this volume is likely to be of very great interest not only to the medical services of the armed forces but to the administrative medical officers and even to the medical profession in general.

Altern und Krankheit—Von Max Bürger. Veb Georg Thieme, Leipzig, 1957, DM 45.

Ageing and Disease (in German)—By Prof. Dr. Max Bürger, Director, Medical Clinic, University of Leipzig. 3rd ed., 684 pp., 348 illustr., Georg Thieme, Leipzig, 1957, DM 45.

The fact that this edition appeared only two years after the previous one is proof of the great interest which problems of ageing arouse nowadays, when in developed countries the expectation of life has doubled within the last 50 years, so that degenerative diseases have vastly replaced infectious ones. But this book is not just another treatise on geriatrics. It is unique in the sense that it is devoted to proving that every physiological as well as every pathological process is determined by the phase of ageing in which it takes place. The author, a leading German physician, founded in 1939 a journal devoted to research on ageing and for more than 30 years he and his pupils have investigated changes caused by ageing—histologically, biochemically, radiologically and, above all, by careful clinical observation. The results are reported in this book.

The general part, in 25 chapters, deals with a variety of interesting topics ranging from the ageing of the inorganic world, of unicellular organisms and metazoa to a systematic investigation of the changes that different tissues undergo due to ageing. Nitrogen, cholesterol, calcium and water content have been estimated at various ages in cartilage, in animal lenses, in the aorta of cattle, horse and man, in placenta, liver, spleen and kidney. About 400 human brains have been minutely analysed as to their dry residue, lipoid spectrum, protein content etc.; similarly, spinal cord and peripheral nerves have been examined. Investigations of bones, skin, hair, nails and teeth conclude the part devoted to static ageing processes. The dynamic

changes have been studied on the manifold cardiovascular and respiratory functions. The influences of age on the haemopoietic system, on blood chemistry, ferment production, metabolism and muscle power, on resistance to infection and immunity, on tolerance to poisons and on the sense organs and, finally, biological age and macrobiosis are discussed on the basis of numerous original investigations and an exhaustive survey of literature, covering more than 100 years and including papers published in 1956.

The special part deals with the course of diseases as influenced by age. Diseases of the lung, of blood vessels and heart, peptic ulcer, diseases of the blood and lymphatic tissue, cancer, liver and biliary tract, diabetes and other metabolic disturbances, diseases of the locomotor system, infectious diseases, nephropathies and diseases of the nervous system, all of them in their dependence on age as well as the influence of heredity on ageing, some surgical considerations and a few wise pages on ageing and maturing of the physician himself are unrolled before the reader's eye, mixing in a most interesting and often unexpected way old experience and new observations to a convincing picture of continuous change from the moment of fertilisation to the hour of death. Authors and subject index cover 27 pages. This is a most stimulating work, well worth an English translation.

Retropneumoperitoneum und Pneumomediastinum—Von Prof. Dr. U. Cocchi, Zürich. Mit einem Geleitwort von Prof. Dr. H. R. Schinz, Zürich. 1957. X, 226 Seiten, 142 Abbildungen in 285 Einzeldarstellungen, 5 Tabellen und 44 erläuternde Zeichnungen, Lex.-8°, Ganzleinen DM 75). (79. Ergänzungsband der "Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin". Vorzugspreis für Abonnenten der Zeitschrift DM 67.50).

Retropneumoperitoneum and Pneumomediastinum (in German)—By Prof. Dr. U. Cocchi, Zürich; with an introduction by Prof. Dr. H. R. Schinz, Zürich. 226 pp., 142 illustr. in 285 figures, 5 tables and 44 explanatory drawings. Georg Thieme, Stuttgart, 1957. DM 67.50.

This monograph deals with two new methods of radiological investigation, of which the former superseded pneumoperitoneum and perirenal gas insufflation because it gives more information and involves less danger; the latter, however, to which only 36 pages have been allotted, should be used with restraint.

After an adequate consideration of pneumoperitoneum and perirenal gas insufflation, the discussion of the retropneumoperitoneum starts with an excellent anatomical introduction, followed by a detailed description of the four different methods or routes of insufflation, tolerance to and by-effects of each of them. The next chapter gives a complete illustrated survey of the normal radiological picture of the retropneumoperitoneum regarding the whole abdomen as well as single organs such as liver, diaphragm, gallbladder, spleen, kidneys, adrenals, pancreas and the other abdominal and pelvic structures. There follow 90 pages about the pathological appearances of kidneys, suprarenal glands, pancreas, liver, spleen, the large abdominal vessels with special emphasis on aneurysms, and a fascinating section on the detection of tumours and their metastases.

The second, much shorter part gives full information about the topographic anatomy of the mediastinum, the spontaneous and artificial pneumomediastinum. The latter can be induced by nine different routes, each of which is concisely described and evaluated; discussions of tolerance and by-effects, the normal x-ray appearance of the pneumomediastinum, indications and contra-indications form the last sections.

The author, who contributed a chapter on the same subjects to "Röntgendiagnostik; Ergebnisse 1952-1956", reviewed in these columns before, is highly qualified by an unusually wide personal experience in the application of these methods and a unique knowledge of the world literature to write an authoritative guide; 1000 references in every possible language fill 20 closely printed pages. Paper and print are perfect; the illustrations are so beautiful and numerous that they form a complete atlas and permit, probably, understanding of the subject matter even without much knowledge of the language.

OBITUARY

Dr. P. Singh

Dr. Parmeshwar Singh, a member of the I.M.A. Sindri Branch, met a tragic death on 2 August 1957 as a result of a truck-motorcycle accident.

Dr. Singh passed the L.M.P. examination from the Cuttack Medical School in 1929 and after a short training in the hospital, started independent practice at Dumka (Santhal Pargana). In 1945 he took up service in the

DR. P. SINGH.

Sindri Fertilisers as the First Medical Officer and next in 1952 joined the Bihar Institute of Technology as its medical officer. He left this job after 2 years and established his own clinic at Sindri.

Dr. Singh was connected with all public institutions of Sindri. He was respected by all for his honesty, simplicity and professional skill.

May his soul rest in peace!

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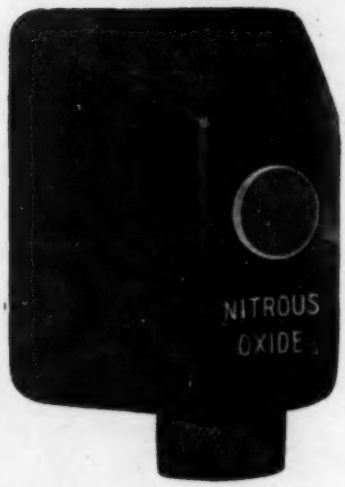

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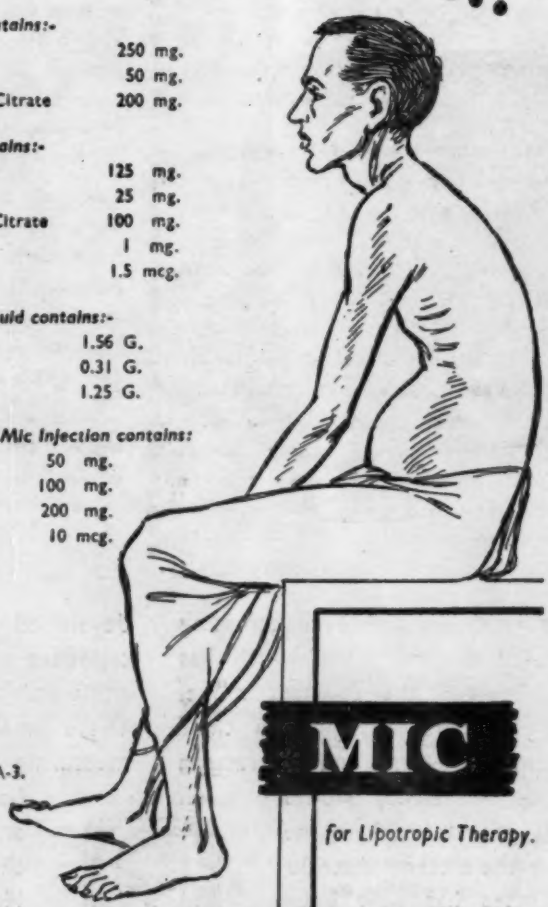

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McCarrison in one of his addresses remarked: "The general dietetic error lies not in quantity, but in quality." Faulty nutrition is no doubt common in this country, but it is not so much lack of food as lack of the right kind of food, particularly vitamins and fats.

In a statistical survey of Vitamin A deficiency —judging by poor dark adaptation—more than half the children from working class homes in England were found to be deficient by Harris and Abbasy in 1939. Both in Africa and India, skin changes due to lack of Vitamin A were present in 80% of some groups of children (Nicholls, L-Indian Medical Gazette : 1933). This is also emphasised in Health Bulletin No. 23 (1956), issued by the Nutrition Research Laboratories, Coonoor. Vitamin A deficiency is the single factor responsible for a large number of nutritional deficiency diseases. The daily allowances for an adult are in the neighbourhood of 3,000 to 4,000 International Units of Vitamin A.

Vitamin A is found in only a very few foods, of which the most common are eggs, milk and butter, and for that reason it is important to realise that their Vitamin A content is not constant, but depends on the diet of the hens and cows. Besides, these animal foods are expensive and beyond the reach of many. Therefore, Fitzgerald Moore, in a practical discussion of the whole problem, concludes that the only hope of a solution is to reinforce local vegetable oils and fats with Vitamin A concentrates. As is well known, the Food Fortification Sub-Committee of the Indian Council of Medical Research thought on the same lines, and recommended that 700 International Units of Vitamin A should be added to every ounce of Vanaspati. This recommendation was accepted by the Government and to Dalda we add 700 International Units of Vitamin A in addition to 56 International Units of Vitamin D.

Fat must be included in ordinary diets—because of its high calorific value and its protein-sparing action. But we have no exact knowledge of the quantity required. It is probably advisable that not less than 45-60 grams (1½-2 oz.) should be consumed daily. Most diets in India are very low in fat.

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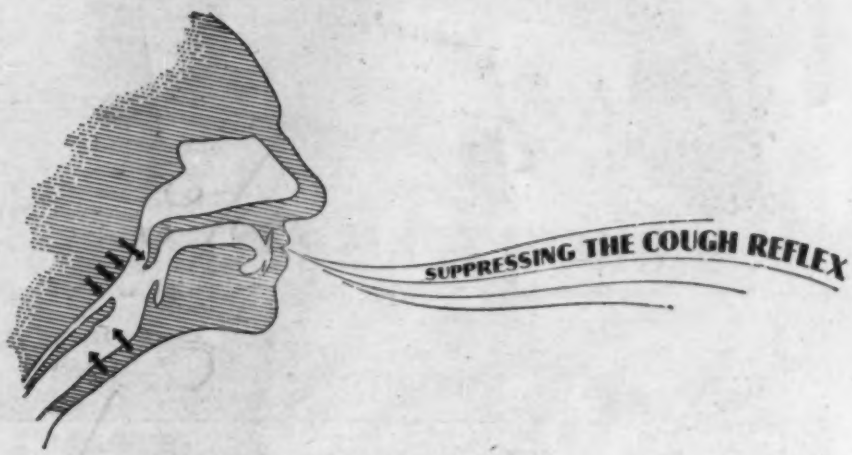

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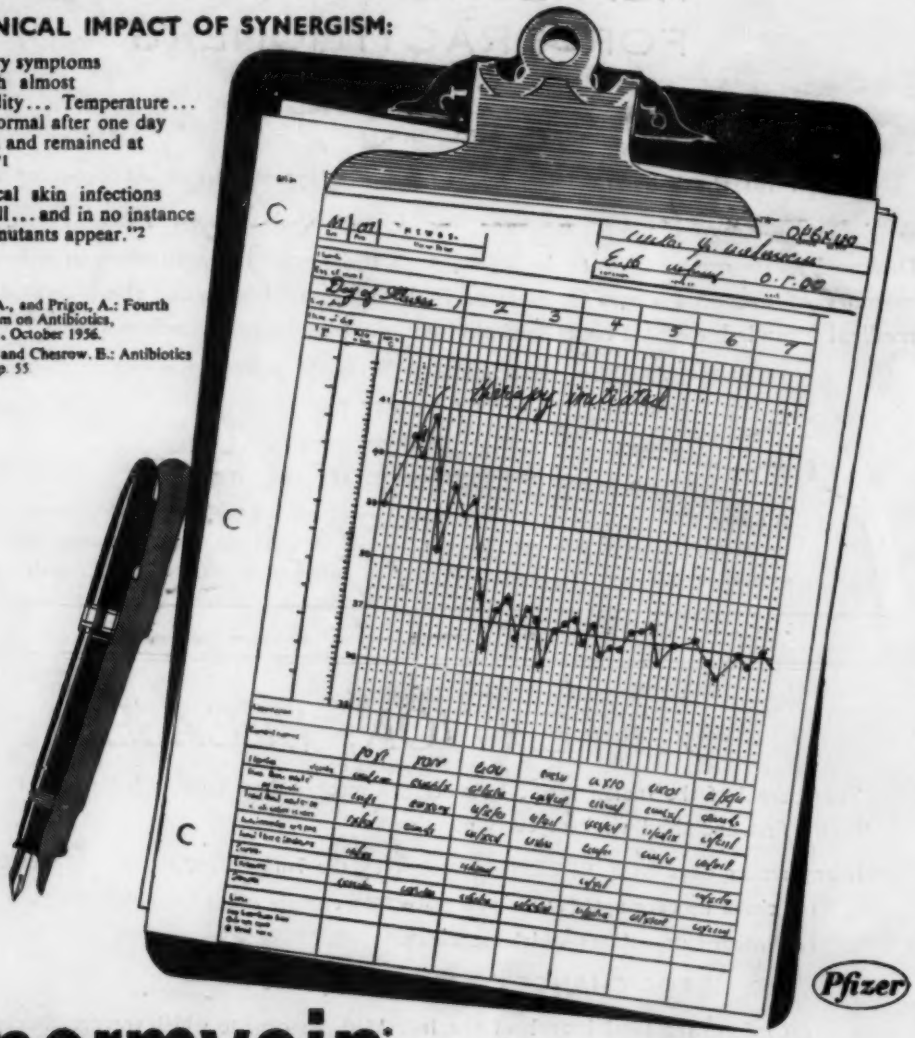
1. La Caille, R.A., and Prigot, A.: Fourth Annual Symposium on Antibiotics, Washington, D.C., October 1956.
2. Winton, S.S., and Chesrow, B.: Antibiotics Annual 1956-57, p. 55



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